The New England
Journal of Medicine

VOLUME 215 AUGUST 20, 1936 NUMBER 8

The Massachusetts Medical Society

SECTION OF DERMATOLOGY AND SYPHILOLOGY

Municipal Auditorium, Springfield, Monday, June 8, 1936

PRESIDING:
Dr. Harvey P. Towle, Boston, Chairman.
Dr. Rudolph Jacoby, Boston, Secretary.

CHAIRMAN TOWLE: The meeting will please come to order. The first business to come before it is the report of the Nominating Committee and the Election of Officers. May we hear from Dr. Boardman, the Chairman of the Committee?

DR. BOARDMAN: The Committee nominated as Chairman Dr. C. Morton Smith, and as Secretary, Dr. J. Harper Blaisdell.

THE CHAIRMAN: You have heard the report of the Committee. What is your pleasure?

A MEMBER: I move that the report of the Committee be accepted and that the Secretary cast one ballot for the Nomination and Election of Officers.

(The Secretary cast a ballot electing Dr. C. Morton Smith, Chairman; and Dr. J. Harper Blaisdell, Secretary.)

THE CHAIRMAN: Before I begin there is one thing I wish to say to you, and that is we will have a round table discussion at luncheon at the Hotel Kimball following this session at approximately 12.45 if there are enough present to have one. I wish the men here who expect to attend would kindly raise their right hands.

(The Secretary recorded the members desiring to attend.)

THE CHAIRMAN: The first paper on the program is by Dr. Francis M. Thurmon, of Boston, on "Bismuth Ethyl Camphorate. Clinical Observations on a New Oil Soluble Bismuth in the Treatment of Syphilis."

BISMUTH ETHYL CAMPHORATE*

Clinical Observations On A New Oil Soluble Bismuth In The Treatment of Syphilis

BY FRANCIS M. THURMON, M.D.†

OF the eighty-odd bismuth preparations that may be offered to physicians for use in the treatment of syphilis, there are two main classifications, namely, the soluble and the insoluble groups. Of the soluble group there are two types: the aqueous solutions and those that are soluble in oil. It is with the latter, an oil soluble bismuth, that this paper deals.

Clinical experience with the bismuth compounds points to the liposoluble preparations as being the best form of this metal for intramuscular injection at seven-day intervals. This is because the oil soluble preparations possess an optimum rate of absorption and elimination and a superior ability to penetrate the tissues. On the basis of absorption and elimination alone the liposoluble preparations lie somewhere between the extremely motile aqueous solutions and the less motile bismuth suspensions.

If a liposoluble bismuth possesses the properties of stability, treponemicidal effectiveness, resistance building qualities, adequacy from the standpoint of serologic response, and manifests a low degree of toxicity when other drugs are not tolerated, then that bismuth should be given careful consideration. The following data represent an eighteen months' study of such a liposoluble compound. This study, then, is a clinical evaluation of a new bismuth synthetic, bismuth ethyl camphorate, which was submitted for clinical testing in August, 1934.

Bismuth ethyl camphorate is a new oil soluble salt of bismuth. It is a pure organic compound made by the interaction of ethyl sodium camphorate and bismuth nitrate. Upon analysis the bismuth content agrees with the theory required by the formula C_{36} H_{57} O_{12} Bi (23.47 per cent Bi). It melts at 57°C. and is soluble in oil and oil solvents.

Acute toxicity experiments using albino rats show the drug to be tolerated intramuscularly in doses somewhat larger than 250 mg. of metallic bismuth per kilogram rat. All of the rats at the 250 mg. dosage survived, while those receiving 400 mg. per kil-

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The Bismuth Ethyl Camphorate used in this study was furnished by The Upjohn Company, Kalamazoo, Michigan.
Read at the Annual Meeting of the Massachusetts Medical Society, Section of Dermatology and Syphilology, Springfield, June 8, 1936.

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ogram did not survive. These results compare favorably with other oil soluble bismuths that have been described for use in the treatment of syphilis in man.

As this drug had not heretofore been used in the human subject, the study was planned for a small group of patients who could be under careful clinical observation and on whom a comprehensive laboratory study might be made. The preliminary period of observation showed that bismuth ethyl camphorate possessed special properties which appeared to justify a more extensive study of the drug. Consequently the investigation has extended over the past eighteen months and includes 230 patients who have received 2,444 intramuscular injections.

CLINICAL MATERIAL

From a clinic with approximately 1800 syphilities under active treatment a series of 230 unselected cases were treated without regard to the stage of the disease. They included nineteen patients with primary; thirty-six with secondary; ninety-one with tertiary asymptomatic; sixty-three with tertiary symptomatic; and twenty-one with congenital syphilis. There were 146 males and eighty-four females. Fourteen were pregnant. Their ages ranged from four to seventy-three years. The decade containing the largest group was the thirty to forty year period (sixty-six patients), while seventy-four per cent of the entire group (171 cases) fell within the twenty to fifty year period.

The tertiary symptomatic group contained sixty-three patients. The incidence and type of syphilis presented by this group were as follows: skin and mucosal, six; bone, four; gumma of thyroid, nasopharynx, sternoclavicular articulation, penis, one case of each; neurosyphilis, thirty-three (tabes, nineteen; paresis, five; taboparesis, two; meningeal, seven); cardiovascular: aortitis early, seven; aortitis with hypertension, seven; aortic insufficiency, eight; aortic aneurysm, four; syphilitic heart disease, six*; eye, twenty.

There were twenty-one patients with congenital syphilis. Of these, two were pregnant; five had an old interstitial keratitis; one an acute interstitial keratitis; one an old chorioretinitis and gumma of the jaw; and one, a female, aged twenty-six years, had an aortic insufficiency and neurosyphilis.

The primary, secondary and tertiary asymptomatic groups were of the usual run of patients for each of these entities.

During the course of treatment, routine ophthalmoscopic and visual field examinations were made. Each patient had frequent chemical and microscopic studies of the urine. Occasional phenolsulphonphthalein excretion tests, and determinations of the nonprotein nitrogen and urea content of the blood, were carried out. Complete blood counts, icteric index and Fouchet tests were made in numerous instances. In these tests no significant variations from the normal were observed which might be attributed to bismuth ethyl camphorate.

*Of the six patients with syphilitic heart disease there was one instance of myocarditis with bundle branch block, three with cardiac decompensation, and two with cardiac hypertrophy.

TECHNIC OF ADMINISTRATION

Bismuth ethyl camphorate is administered in 1 cc. doses intramuscularly. The drug is a stable, clear, oily solution, each cubic centimeter containing benzyl alcohol 0.02 gm., elemental bismuth 0.04 gm., and camphor 0.10 gm., in sweet almond oil. The inner angle of the upper outer quadrant of the buttock is the preferred site of injection. Treatments are alternated between the two buttocks.

The patients best tolerated the 1 cc. dose. Higher dosage of 1.5 cc. and 2 cc. was well tolerated by some patients, while others manifested local pain, gingivitis, occasionally a mild dermatitis and seldom evidence of a transient renal irritation.

Infants and young children permitted larger amounts in proportion to body weight than did adults. The ratio of a 10 mg. dose for infants up to twenty-five pounds seemed to be the optimum amount for that weight. Heavier children easily permitted a 20 mg. to 30 mg. dose, while those beyond eighty pounds body weight were treated with the adult dosage, attention being given to the urine and gums.

A course of heavy metal therapy in this clinic constitutes twelve injections. The fifty-five patients with primary and secondary syphilis received arsphenamine previous to the administration of bismuth ethyl camphorate, as there seemed to be no justification for starting them on bismuth.

Clinic routine for treating early syphilis calls for immediate administration of arsphenamine, each patient receiving three injections a week for the first two weeks, two injections a week for the second two weeks, and one injection a week for the succeeding two weeks, so that at the end of the first six weeks of treatment each patient has received twelve intravenous injections of an arsenical preparation.* Then, without an intervening rest period, intramuscular therapy is instituted, and in these cases each patient received an injection of bis-

*Arsphenamine therapy as applied here denotes the following: Clinic routine calls for the use of arsphenamine in all cases whenever possible. The adult dose ranges from 0.2 gm. to 0.4 gm., rarely going above the latter figure. Should untoward reactions to arsphenamine occur, then neoarsphenamine is employed, the dose being 0.3 gm. to 0.6 gm. Should untoward reactions to the latter occur, then silver arsphenamine becomes the drug of choice, the dose ranging from 0.1 gm. to 0.3 gm. Through the past ten months the drug mapharsen has been added to this routine, since it has been found that many patients will tolerate mapharsen when toxic reactions to the above arsenicals have occurred.

muth ethyl camphorate at seven-day intervals for a total of twelve injections. This is considered to constitute one course of treatment. Regardless of the patient's serologic reactions and provided the clinical progress has remained uneventful, treatment is continued until two additional courses have been administered. With regular attendance this period of continuous medication covers the first sixty-six weeks of observation, during which time the patient has received thirty-six injections each of an arsenical preparation and of bismuth, which in this instance was bismuth ethyl camphorate. These seventy-two injections are considered to be the minimum therapy any patient with primary or secondary syphilis should receive.

The remaining patients in this series (175) comprised the asymptomatic, congenital and tertiary symptomatic groups. Exclusive of neurosyphilis, they received bismuth ethyl camphorate in blocks of twelve injections alternating with twelve injections of one of the arsenical preparations, each treatment being administered at seven-day intervals. Patients with neurosyphilis were usually treated with tryparsamid, with an occasional substitution of metallotherapy and one of the arsphenamines as mixed treatment.

The state of their physical condition, exclusive of sensitivity to bismuth, formed no contraindication to the recommended dosage of 1 cc. A few instances of recurrent syphilis with resistant lesions required intensive medication. In these instances bismuth ethyl camphorate was administered twice each week, an arsenical drug every third day, and mercury and potassium iodide by mouth, over periods of two to four weeks if necessary. This was accomplished without undue toxic effect and with a resulting involution of the recurrent lesions.

Occasionally prolonged treatment with one drug was necessary because of sensitivity to other preparations. For this reason twenty-one patients received from fifteen to twenty consecutive injections, and another group of fifteen patients received from twenty to twenty-five injections respectively of bismuth ethyl camphorate without toxic effect. One patient, a male, aged twenty years, sensitive to all arsenicals, developed an acute interstitial keratitis for which he received twenty-nine consecutive injections of bismuth ethyl camphorate (40 mg. each) without toxic effect and with a clearing of the eye situation in six weeks.

With respect to prolonged treatment using the same drug, it is believed that with bismuth ethyl camphorate as with all heavy metals and all arsenicals, it is not advisable to continue treatment with the same drug too long lest that drug lose its effectiveness. This is amply illustrated in clinic practice where serorelapses, recurrent mucocutaneous eruptions, and the development of tertiary lesions occur altogether too frequently where a single one of these preparations is used to the exclusion of all others.

Bismuth ethyl camphorate has proved to be a valuable drug in the serofast or seroresistant group of cases, since many of these patients show negative blood tests after its use whereas previously for years the serology* had remained persistently positive. However, it is important to remember that continued mixed treatment is of the greatest value in order to hold the serologic ground gained, lest the change from positive to negative be only temporary. This observation applies to all forms of chemotherapy for syphilis.

RESULTS

Pregnancy.—There were fourteen cases of pregnancy which were distributed as follows: congenital, two; secondary, five; tertiary asymptomatic, five; and tertiary symptomatic, two. In each of these instances it was possible to administer treatment through the last five months of pregnancy. They received regular treatment at seven-day intervals up to term, starting with a twelve injection course of bismuth ethyl camphorate which was followed by arsphenamine intravenously. The bismuth ethyl camphorate was received without ill effect. Each patient produced a full-term child with no stigmata of congenital syphilis. Certain laboratory studies on the infants were completed within the first three months following birth. They revealed negative Hinton, Wassermann and Kahn reactions on the blood, and x-rays of the long bones were normal. Although this period of observation is too short to evaluate fully the effect of this treatment upon the offspring of patients with syphilis, it may be said with certainty that there were no demonstrable toxic effects from the drug upon either the mother or fetus, and each of the pregnancies went to full term.

Serology.—The serologic results are summarized in table 1. The effect of bismuth ethyl camphorate in producing a serologic change is perhaps one of the strongest points for its use. Of the 180 patients on whom serologic data were available at the beginning and end of bismuth ethyl camphorate therapy, the Hinton, Wassermann and Kahn reactions remained negative in twenty-five instances throughout the period of observation. Not only does this new oil soluble preparation seem to hold the serologic ground gained by other methods of treatment, but in addition, with its routine use as outlined, a serologic change was produced in fifty per cent of the remaining 155 cases.

*The term serology as used in this paper denotes the routine use of the standard tests for the Hinton, Wassermann and Kahn reactions.

TABLE 1

SEROLOGIC CHANGES NOTED FOLLOWING THE USE OF BISMUTH ETHYL CAMPHORATE IN THE ROUTINE TREATMENT OF 180 PATIENTS WITH SYPHILIS*

Stage of Syphilis	Number of Cases	Serology Completely Negative Throughout		Hinton				Serologic Changes Wassermann				Kahn			
				Pos. to Neg.		Dbt. to Neg.	Pos. to Dbt.	Pos. to Neg.		Pos. to Dbt.		Pos. to Neg.		Pos. to Dbt.	Dbt. to Neg.
		Cases	Per Cent	Cases	Per Cent	Cases	Cases	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Cases
Primary	19	13	68.4	6	31.6	0	0	5	26.3	0	0	5	26.3	0	0
Secondary	31	4	12.9	6	19.3	2	4	11	35.4	1	3.2	11	35.4	0	0
Tertiary															
Asymptomatic	65	3	4.6	9	13.8	2	5	6	9	2	3	6	9	1	3
Tertiary															
Symptomatic	52	4	7.7	3	5.7	1	1	4	7.7	2	3.8	8	15.3	2	0
Congenital	13	1	7.7	1	7.7	0	0	0	0	0	0	1	7.7	1	1

*Additional data bearing on these serologic changes are appended in table 2.

In the group of 180 patients on whom complete serologic data were obtained, the Hinton test was persistently negative in twenty-six, the Kahn in fifty-four and the Wassermann in ninety-four cases respectively. This, to say the least, is illustrative of the comparative degree of sensitivity of these three tests as performed in the laboratory of The Boston Dispensary.

The reversal of positive and doubtful serologic reactions to negative is of considerable significance, especially as it relates to the Hinton reaction. It is the experience of this clinic that the Hinton reaction is more difficult to render negative than either the Kahn or Wassermann. The degree with which this was accomplished is illustrated in table 1. The changes from positive to negative were essentially the same in all three tests.

The reversal of negative or doubtful serology to positive is also of some significance. The eleven instances where this occurred in this series are appended in table 2. They are strongly suggestive of a possible provocative use of the drug.

EFFECT UPON VISIBLE LESIONS

An evaluation of the effectiveness of bismuth ethyl camphorate in the treatment of early syphilis was necessarily incomplete because of the clinic policy of starting these patients on one of the arsphenamines. In only one instance was there an opportunity to observe, even partially, the effect of the drug in primary syphilis. In this case, following the second injection of the arsenical used, the patient experienced a severe prolonged reaction characterized by nausea, vomiting, anorexia, dermatitis, fever and jaundice. The penile lesion was of a deep ulcerative type that had barely begun to involute. Bismuth ethyl camphorate (40 mg. doses) was administered at three-day intervals. Within ten days the toxic manifestations had disappeared and at the end of fourteen days the healing of the ulcerative defect and involution of the infiltrate was accomplished. Later an arsenical preparation again precipitated toxic reactions.

There were four clinical relapses as shown by the recurrence of cutaneous or mucosal lesions, due either to irregular and insufficient treatment or occurring during bismuth salicylate therapy. These recurrent lesions involuted rapidly under bismuth ethyl camphorate therapy (40 mg. dose) at four-day intervals, and completely disappeared by the time of the fourth injection.

An acute interstitial keratitis was brought under control following the sixth injection of bismuth ethyl camphorate when the recommended 40 mg. dose at seven-day intervals was used.

The tertiary manifestations were usually those of a serious nature. Of the visible type sixteen patients with optic atrophy ranging from slight pallor of the nerve head to complete atrophy in one or both optic nerves were of interest. Often during treatment with the arsphenamines these patients rapidly lose their visual acuity and progress to complete blindness unless carefully controlled. We have yet to see this occur under intramuscular bismuth or mercury therapy alone. It did not occur in the sixteen cases cited here. Each patient tolerated bismuth ethyl camphorate well. In eight of the sixteen where pallor of the optic nerve was slight there was no change noted in the visual fields, but there was measurable improvement in visual acuity.

A single instance of papilledema due to syphilis was treated with bismuth ethyl camphorate. This patient, a male, aged 36, had neurosyphilis. His vision was restored to normal through use of the new liposoluble bismuth administered at seven-day intervals. Later he proved to be intolerant to the arsphenamines. Nitritoid crises were caused by neoarsphenamine and arsphenamine precipitated a toxic hepatitis with icterus. Bismuth ethyl camphorate was tolerated very well.

One patient, a female, aged 58, entered with an ulcerative lesion involving the thyroid gland. There was healing and scarring in some parts of the involved area while other portions showed destructive ulceration. The entire process seemed matted together and bound down into a single immovable unit. Portions of the thyroid gland were firm and hard. Biopsy was refused. The Hinton, Kahn and Wassermann reactions were repeatedly positive. Six injections of bismuth ethyl camphorate (40 mg. each) at seven-day intervals produced practically complete involution of the lesion. The case could not be followed to completion, since, for social reasons, she was transferred to another clinic. Follow-up there indicated total healing of the area within the next few weeks.

Patient A. R., a female, aged 43, was an interesting problem case of bone and cutaneous manifestations. She entered with secondary syphilis. Nitritoid crises were experienced under arsphenamine, neoarsphenamine and bismarsen. A toxic hepatitis with icterus was precipitated by arsphenamine. Headaches, dizziness and loss of consciousness followed bismuth salicylate on two occasions. A secondary mucocutaneous relapse occurred during mercury succinimide therapy, the rash involuting under small doses of silver arsphenamine. Yet no sooner had the recurrent lesions disappeared when hydrarthrosis of both knees, osteomyelitis of the right tibia, and ulcerative lesions of each leg developed. Potassium iodide produced an iodide eruption. Twelve injections of bismuth ethyl camphorate (40 mg. to 60 mg. each) administered at three-day intervals were well tolerated. The edema, pain and redness of the knees subsided, the cutaneous lesions healed, but the draining sinus of the osteomyelitis continued to discharge. It was only after the patient received ten fever treatments in the Kettering Hypertherm consisting of 28 hours of fever between 105° and 106° and 6 hours between 104° and 105°, that the osteomyelitis cleared. After the first three treatments there was distinct improvement in the bone lesion as evidenced by x-ray. Further examination after five treatments showed denser bone in the region of the lesion and after the complete series of treatments the bone condition remained cleared and the patient felt well and healthy again.

Patient No. 350239, a female, aged 46, entered with "myocarditis" and a gumma of the right leg. Twenty-four consecutive injections (40 mg. each) of bismuth ethyl camphorate were administered at seven-day intervals. The gumma healed in four weeks. There were no toxic manifestations and the urine remained normal throughout treatment.

Patient No. 153940, a male, aged 58, with tabes dorsalis developed a gumma of the left testicle while undergoing treatment with tryparsamid. Twelve injections of bismuth ethyl

TABLE 2

SEROLOGIC CHANGE FOLLOWING THE USE OF BISMUTH ETHYL CAMPHORATE IN ELEVEN PATIENTS WITH SYPHILIS

Test	Cases	Serologic Change	Type of Syphilis
Hinton	One	Negative to Positive	Tabes dorsalis and optic atrophy
Hinton	One	Negative to Positive	Recurrent secondary syphilis
Hinton	One	Doubtful to Positive	Paresis
Hinton	One	Doubtful to Positive	Asymptomatic syphilis
Wassermann	One	Doubtful to Positive	Tabes dorsalis
Wassermann	One	Negative to Doubtful	Aortitis
Kahn	One	Negative to Positive	Paresis
Kahn	One	Doubtful to Positive	Aortitis
Kahn	One	Doubtful to Positive	Charcot's knees
Kahn	One	Negative to Doubtful	Congenital
Kahn	One	Negative to Doubtful	Asymptomatic syphilis

camphorate were administered, and the gumma disappeared after the eighth injection.

A twenty-two year old male with secondary syphilis developed an ulcerative scrotal lesion that resisted intensive arsenical and heavy metal therapy. The lesion cleared after six injections of the new liposoluble preparation.

Patient No. 345843, a male, aged 28, had tertiary cutaneous syphilis with skin lesions over the trunk resembling dermatitis herpetiformis and ulcerations on the legs. These areas cleared after the sixth treatment with the new drug.

There were numerous instances of the types indicated above where visible lesions of syphilis were of concurrent appearance with more serious manifestations of the disease. The progressive manner in which the new oil soluble bismuth caused these lesions to disappear seemed to leave no question of doubt as to the therapeutic effectiveness of the drug.

TOXICITY

The toxic effects of bismuth ethyl camphorate are summarized in table 3. They are compared with the untoward effects produced by bismuth salicylate, a standard insoluble bismuth salt suspended in oil. The 180 patients of the bismuth salicylate series were regular clinic cases under routine treatment. The comparison shows the liposoluble bismuth in a favorable light.

TABLE 3

TOXIC EFFECTS NOTED IN USE OF BISMUTH ETHYL CAMPHORATE AND BISMUTH SALICYLATE IN TREATMENT OF SYPHILIS

Signs and Symptoms	Bismuth Ethyl Camphorate 230 Cases	Bismuth Salicylate 180 Cases
Local Pain	20	30
Leg Pain	1	1
Generalized Aches and Pains		4
Bitter Taste—Aching Gums	2	1
Metallic Deposit in Gums	2	12
Headache, Sore Throat		4
Gastro-Intestinal*	1	5
Nitritoid Crises†	1	1
Dermatitis‡	2	1
Jaundice		1

*Nausea, vomiting, diarrhea, cramps.

†Patient stated following the third and fourth injections of bismuth ethyl camphorate that chills and fever occurred. Bismuth salicylate was tolerated very well. Following the fourth injection of bismuth salicylate, chills and fever occurred, later jaundice appeared and the liver was palpable. Bismuth ethyl camphorate was started while the liver was still palpable, jaundice visible, icteric index 20, and these signs cleared.

‡With bismuth ethyl camphorate the dermatitis was a transient erythematosquamous eruption of face and neck, while that caused by bismuth salicylate was a miliary folliculo-papular eruption of trunk and extremities.

Local Irritation.—The local tissue reaction is generally mild. In only eight instances out of 230 cases was it necessary to transfer the patient to some other form of treatment for this cause. Approximately ten per cent of the patients complained of local stiffness or soreness lasting from ten to twenty-four hours and rarely for more than forty-eight hours after injection. Usually after the initial two or three injections no further pain was noted. No demonstrable local inflammatory changes and no abscess formation occurred in 2,444 injections.

Systemic Reactions.—The new drug has a low toxicity from the general systemic point of view. Albuminuria or other evidence of renal irritation such as casts and red blood cells were observed in only two instances.* One patient, a male, aged 28, with tabes dorsalis and optic atrophy showed the faintest possible trace of albumin and an occasional cast following the ninth injection of bismuth ethyl camphorate. The other patient, a male, aged 52, with cardiovascular syphilis and hypertension showed a few hyaline casts, an occasional red blood cell and a rare white blood cell but no albumin, following the thirteenth injection of bismuth ethyl camphorate. These changes were of temporary significance for in each instance the urine cleared within three weeks after discontinuing the heavy metal. In the remaining 228 patients the urine (684 analyses) remained normal throughout.

In none of the patients was there evidence of liver damage, stomatitis or reactions suggesting anemia or aleukemia hemorrhagica. With exception of two patients who showed a transient conjunctival hyperemia there were no toxic ocular manifestations. Treatment in these two patients was continued. In all cases where dental hygiene was good there was no evidence of bismuth deposit at the gingival margins. An occasional patient would notice a taste of camphor shortly after treatment but this effect was transient, not an objectionable feature and lasted only a few moments. The single recorded instance of nitritoid crisis is of difficult evaluation. It is based entirely upon the patient's statement, namely, that a few hours after the third and fourth injections of bismuth ethyl camphorate she had chills and fever which incapacitated her for the remainder of the day of treatment.

During the early period of the study when larger amounts (60 mg. to 80 mg.) than the recommended dose (40 mg.) were used, the drug did seem to possess potential possibilities of toxicity, that is to say, the untoward effects noted in table 3 were slightly magnified, yet in direct proportion to the larger dose the therapeutic effectiveness seemed to be increased as was noted in serologic reversals and the rapid clearing of visible tertiary lesions.

Lack of Toxicity.—The best measure of a lack

*Routine urinalyses were done at the beginning, middle and end of each course of twelve injections of bismuth ethyl camphorate, and at the beginning and end of each block of intravenous therapy.

of toxicity is perhaps expressed by the great number of instances where bismuth ethyl camphorate could be used with comfort and safety when other preparations caused toxic or ill effects. There were sixteen instances where bismuth salicylate was discontinued because of local or systemic reaction. Mercury succinimide caused folliculo-papular eruption or abdominal cramps and diarrhea in four cases. Bismarsen precipitated nitritoid crises in five of the patients. Iodo-bismuthate of quinine accentuated general aches and pains in two cases and had to be discontinued. In each of these instances bismuth ethyl camphorate was well tolerated when the dose was kept within the recommended therapeutic range.

In this connection patient, B.D. No. 340878, a female, aged 29, with secondary syphilis is interesting. Under arsphenamine she developed a dermatitis. Bismuth salicylate caused severe aching pains and edema in the hands and arms. Under mercury succinimide a hepatitis with icterus occurred. The liver was palpable three fingers below the costal margin and the gums were spongy, blue and showed a sanguineous ooze. A terrific nitritoid reaction to sodium thiosulphate occurred. During this distressing period she was started on bismuth ethyl camphorate and tolerated it very well, receiving twelve doses without untoward effect, though she did complain of mild itching following the eighth injection. As there was no rash or dermographia, treatment was continued with a resulting disappearance of the toxic and syphilitic manifestations.

In the series of 230 patients many of them manifested toxic reactions of various types to the arsenical preparations. Of these untoward manifestations forty-nine patients experienced nitritoid crises to one or more of the arsphenamines including bismarsen. There were eleven instances of hepatitis with icterus, nine of dermatitis, and two of toxic ocular reactions including neuroretinitis.* During the acute stage of each of these toxic manifestations the offending arsenical was withdrawn and treatment for syphilis was carried on with bismuth ethyl camphorate for a period of three to five months. The toxic manifestations disappeared and clinical progress continued uneventful under the new oil soluble preparation. In this respect bismuth ethyl camphorate is no different than other of the standard bismuth preparations.

ABSORPTION AND ELIMINATION

As this problem was a clinical evaluation of a new oil soluble bismuth no special studies were directed toward absorption and elimination. However, judging from the therapeutic effectiveness of the drug as measured by the clearing of visible cutaneous lesions of recurrent and late syphilis, serologic reversals, the relief of precordial and vague "rheumatic" tertiary pains, the restoration of a more forceful myocardium after cardiac failure and the occasional instance of bismuth deposit in the gingival margins or the taste of camphor following injection, it seems safe to assume that the drug was absorbed and therapeutically active.

In a few cases where x-ray examination of the injected areas was done as recently as six weeks after the last injection of a series of twelve intramuscular treatments at seven-day intervals, the films showed no shadow of bismuth retention.

SUMMARY AND CONCLUSION

Bismuth ethyl camphorate, a new oil soluble bismuth, is described. The dose, technic of administration and results obtained in the treatment of 230 patients (2,444 injections) are presented. The clinical material from which the data are derived consisted of fifty-five cases of early syphilis, twenty-one congenital, sixty-three with tertiary symptomatic and ninety-one in the latent or asymptomatic stage of the disease. There were fourteen cases of pregnancy.

Each cubic centimeter of bismuth ethyl camphorate contains 40 mg. of elemental bismuth. This amount constitutes the recommended dose which routinely is administered at seven-day intervals, but should intensive treatment be desired the intervals may be shortened to three days.

The results as herein presented indicate that bismuth ethyl camphorate, despite its low bismuth content, is an extremely valuable drug in the treatment of syphilis. It is a safe drug to use. Therapeutically, it is at least equal and in many respects superior to other preparations in the heavy metal series.

Bismuth ethyl camphorate is an exceedingly valuable adjunct to the arsphenamines in the treatment of early syphilis. Used in doses within the therapeutic range, it is of very low toxicity. The number of serologic reversals, the rapid clearing of visible lesions and the ability of patients to tolerate the drug when other preparations are ill tolerated, bespeak its usefulness.

Bismuth ethyl camphorate is well borne by children and in pregnancy. The absence of therapeutic shock and paradoxical effects in vital structures make it a valuable preparation in the treatment of cardiovascular syphilis and in the toxic ocular, hepatic and cutaneous reactions. In neurosyphilis, so far as this small series goes, it is a valuable adjunct as mixed therapy for interrupting the continuous use of tryparsamid.

*Identical with that described by Skirball, J. J., and Thurmon, F. M.: Ocular reactions due to arsphenamine; report of 20 cases. Am. J. Syph. & Neurol. 19:197 (April) 1935.

DISCUSSION

THE CHAIRMAN: This paper is now open to discussion.

DR. CHARLES C. DENNIE, Kansas City, Missouri: I have had no experience with this type of bismuth which has just been reported, but I was extremely interested in the results that have been secured, especially in some of the cases of relapses, and in relapses from other types of therapy. It has always been my opinion that any time where we have relapses either going into the treatment or shortly after the cessation of treatment, the patient voluntarily using the treatment, that the relapses have been due to a lack of response upon the part of the patient. In other words, it must go hand in hand with the active treatment, and we have been able to show by our experience that that is true. In the case of neuro relapses especially does that occur under active treatment, and we are enabled to cause disturbance of these lesions by stimulating motivity of the patient, and that may be done in several ways. We have also noted then with reference to lesions disappearing, as they do in a large majority of cases, that if those patients are left alone those lesions will make their appearance again, in fact sometimes more severely than they did originally. We have found that after a few days' course of hyperpyrexia, or whatever you may have, that same type of treatment that was used without success before the introduction of hyperpyrexia responds rapidly, and so far as we know permanently.

THE CHAIRMAN: Are there any others who wish to speak on this subject? If not we will pass to the next paper, which is "'Mycoses.' Fungus Diseases of the Skin and Internal Organs," by Dr. J. H. Swartz, Massachusetts General Hospital, Boston.

THE ROLE OF FUNGI IN MEDICINE*

BY J. H. SWARTZ, M.D.†

MYOLOGY is no longer a mysterious subject known only to few. It has been proved to be a part of medicine just as bacteriology, physiology, and so forth. Some knowledge of mycology is necessary for a better understanding of disease.

In this paper an attempt will be made to discuss the elements of mycology and its application not only to dermatology but to medicine in general.

The subject of mycology to many conveys the idea that it applies to only one disease, namely "athlete's foot". The so-called athlete's foot, which by the way is a misnomer, represents only one condition that can be caused by fungi.

To make this paper more explicit an attempt will be made to divide it as follows:

1. History
2. Classification of fungi
3. Diagnosis
4. Allergy and fungi
5. Hematogenous dissemination of the dermatophytes
6. Occupational dermatoses and fungi
7. Fungi and internal medicine
8. Treatment

Time and space will not permit giving a historical account of pathogenic fungi. Furthermore, I do not believe it is necessary, since many papers on this subject have already been published. Reference can be made to Dr. Greenwood's[1] excellent paper read before this section last year. However, a few remarks are appropriate.

History.—The history of mycology dates back to the reign of Charles II when Hook, with a lens of his own making, carefully examined the blight of the damask rose, and illustrated his findings. Up to the latter part of the eighteenth century, progress was slow. The men of that time who made important investigations were Malpighi, Ray, Micheli, Linnaeus, Lightfoot, Pelham, Butsch, Bulliard, and others.

From 1800 progress has been much more rapid, but it was not until Ramak, in 1837, discovered the parasitic fungi in ringworm that particular attention was paid to the microfungi as possible factors in the causation of human ills.

One hundred and three years ago Schoenlein discovered that favus, at that time named porrigo lupinosa, was caused by a fungus. For the first time the concept of exogenous parasitory genesis of human disease was elevated to clear reality from the realm of mystic speculations. From 1841 to 1844 Gruby described the etiologic agent of thrush, of favus (independently of Schoenlein), of sycosis barbae, parasitaria, and of trichophytosis. He differentiated the various fungi, recognized their etiologic relationship with definite diseases and evaluated the importance of his discoveries for the genesis and therapy of contagious diseases. The full importance of this will be appreciated when one realizes that these dermatoses were at that time classed as manifestations of diabetic or hereditary diseases. In 1890, fifty-seven years later, Sabouraud applied the methods of Koch and Pasteur to the field of dermatomycoses. He further attempted pure cultivation of mycologic species, recognition of their plurality and specificity and co-ordination of the specific relationship between the clinical picture and the species of the fungi. Later Bloch and Jadassohn and their students developed the biologic phase of dermatomycoses. This work is still being done today. More will be said about this phase in the discussion of allergy and fungi.

*Read at the Annual Meeting of the Massachusetts Medical Society, Section of Dermatology and Syphilology, Springfield, June 8, 1936.

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Classification of Fungi.—No attempt will be made to give a strict botanical classification; first, because it is not practical for our purpose, secondly, because the classification is still chaotic, and thirdly because I am not a botanist. However, an attempt will be made to give a practical and useful classification with apologies to the botanist for not adhering strictly to botanical rules.

Fungi may be divided into two large divisions:

I. Myxomycetes (vegetative body under form of a multinucleated, naked plasmodium).
II. Eumycetes (vegetative body usually filamentous).

The fungi pathogenic to man usually belong to Class II which may be further subdivided as follows:

1. Phycomycetes. The pathogenic species reproduced by zygospores. The mycelium is multinucleate and often nonseptate.
2. Basidiomycetes. Reproduction is by means of basidiospores. The mycelium is septate, and either binucleate or uninucleate.
3. Ascomycetes. Reproduction by means of ascospores. The mycelium is septate when present and usually 2-5 nucleate in pathogenic species.
4. Hyphomycetes or fungi imperfecti. Reproduction is by free-borne spores (conidia) that are never contained in an ascus. The mycelium is septate, and usually uninucleate. Sexual reproduction absent or unknown (whence the name imperfecti).

Most fungi pathogenic to man belong to either the ascomycetes or hyphomycetes which, from a clinical standpoint, can be further subdivided into

a. yeasts and yeast-like organisms (endomycetales)
   (1) saccharomycetes (true yeasts)
   (2) cryptococcus
   (3) monilia
   (4) endomycetes
   (5) coccidioides
b. Ringworm fungi (Gymnoasceae)
   (1) microsporon (Lanosum [animal]) (Audouini [human])
   (2) achorion (Quinckeanum) (Schoenleini)
   (3) trichophyton
      ectotrichophyton, e.g., T. gypseum
      megatrichophyton T. rosaceum
      favotrichophyton T. ochraceum T. violaceum
      eutrichophyton
      neoendothrix T. cerebriform
      endothrix T. crateriforme T. acuminatum
   (4) epidermophyton.

The organisms which cause sporotrichosis and actinomycosis belong to the family of fungi imperfecti.

Diagnosis.—The diagnosis of fungus infection whether it be of the skin or any other organ is not simple. It must be remembered that the finding of a fungus, particularly a yeast-like organism, in the material examined does not always mean that the organism found is the causative agent of the pathology in question. One must bear in mind the fact that the organism may be found either under normal conditions or as a secondary invader; for example, the finding of a yeast-like organism in the sputum, stools, or even on the skin. Before considering it a pathogen in the case in question its pathogenicity by animal experimentation, and so forth, must be established.

A diagnosis of fungus infection of the skin is made by (1) clinical findings, (2) direct microscopic examination and (3) by cultural studies. It may be well at this point to discuss the method of direct microscopic examination of the skin.

The most common procedure is to use a clearing agent such as potassium hydrate, xylol, chloral hydrate, or glycerine, to permit a microscopic examination of the skin scales. Of these, potassium hydrate is the most commonly used and is by far the most effective. However, because of the artefacts such as crystals, fat globules, and the mosaic fungus, the examiner has to use an unusual degree of caution to avoid errors in interpretation of microscopic findings. The author therefore recommends the following technique of Swartz and Conant[2] which eliminates many of the artefacts. After the preliminary treatment of the scales with 10 per cent potassium hydroxide, they are transferred to a watch crystal and washed with water. When the action of the potassium hydroxide is stopped, in two or three minutes, the bits of scales are gently heated in a drop of lactophenol cotton blue and a cover glass pressed on to the preparation. The clearing action of the potassium hydroxide is continued by the lactophenol and the epidermal cells receive a light bluish stain while the granular protoplasmic content of the fungus is heavily stained. In the case of thick scales or nail material a 1 per cent solution of cotton blue in 70 per cent alcohol is used, and the material is then mounted in clear lactophenol cotton blue. This method is valuable not only in the case of distinct well-defined fungus hyphae, differen-

tiating them better than potassium hydroxide alone, but it is especially advantageous in cases where yeast-like budding cells appear in preparations. In such cases the use of potassium hydroxide alone requires the greatest of caution, for many times fat globules also assume such forms and a positive diagnosis must be given with reservations. When, however, such preparations are stained with lactophenol cotton blue, after treatment with 10 per cent potassium hydroxide the scales are sufficiently cleared and the artefacts are not present while the stained budding yeast-like cells are easily recognized.

Allergy and Fungi.—Under the topic of allergy and fungi we have to consider, (1) fungous infections of the skin and its appendages with a resulting eruption which does not show the presence of fungus on direct microscopic examination or on cultural studies. These eruptions are termed "ides". They may vary in type and may be found on the extremities or elsewhere. For example, the lichenoid eruption that may occur with kerion. Fever and constitutional symptoms have been reported.[3]

The first notice of generalized eruptions occurring in connection with focal mycotic infection was taken by Jadassohn, who, in the discussion of Bloch's paper on trichophytosis, described several cases of kerion, in which spiny lichenoid papules were scattered over the trunk. Since then numerous references on the subject have appeared in literature but time and space will permit only a brief mention. Particular reference is made to the excellent papers by Dr. Charles M. Williams.

Numerous reports are found in the literature on the scratch and intradermal tests to trichophytin and oidiomycin but the interpretation varies. However, a good working rule based upon the various findings may be said to be as follows: A positive scratch or intradermal test to trichophytin indicates either a present or past infection. One must remember that an infection in the past may still give a positive test although the present dermatologic condition is not at all related to the test. A negative test, however, is of much greater importance, since it frequently rules out the possibilities of infection. In other words, the trichophytin test is quite comparable to the tuberculin test. Sulzberger and Lewis [4] by means of contact or patch tests with trichophytin demonstrated that products of fungi are capable of causing an eczematous eruption on a hypersensitive skin. Sulzberger and Kerr[5] also recorded a case of a man with tinea of the hands and feet who gave immediate marked urticarial, wheal reactions to intradermal trichophytin tests. With this patient's blood serum they were able passively to transfer the urticarial trichophytin hypersensitiveness to the skin of normal nonsensitive individuals, thus demonstrating the presence in the blood of Prausnitz-Küstner antibodies of specific reagins. Wise and Sulzberger[6] reported the case of a patient with dermatitis and occasional attacks of urticaria, asthma, and hay fever in whom an intradermal test with trichophytin produced an acute attack of hay fever and a generalized urticaria necessitating the administration of epinephrin for relief.

(2) Sensitization to the fungi found in the dust (house and mattress). Storm van Leeuwen[7] was the first to call attention to the importance of mold allergens in the causation of asthma. He attributed the climatic type of asthma so prevalent in Holland to products of the growth of molds, yeasts or bacteria which he termed "climate allergens or miasms". Storm van Leeuwen worked with six different molds, namely, *Aspergillus flavus, Aspergillus fumigatus, Aspergillus nidulans, Aspergillus niger, Mucor,* and *Penicillium,* and by testing his asthmatics intracutaneously with extracts of these molds, found about 50 per cent of them sensitive to mold allergens. Hansen,[8] in Germany found that 15 per cent of his asthmatic patients gave positive reactions to one or more of the following molds: *Aspergillus fumigatus, Aspergillus niger, Penicillium glaucum,* and *Aspergillus nidulans.* He was able to reproduce asthmatic attacks in a number of these patients with spores of the reacting molds.

Hopkins, Benham, and Kesten[9] were the first in the United States to report a case of asthma due to a fungus (alternaria). The patient, in addition to being markedly sensitive to alternaria, gave definitely positive skin reactions to several other skin molds, including *Aspergillus nidulans* culture from an eczematous lesion on his leg. In this connection it may be stated that some years previously Niethe,[10] and Hilgermann[11] had attributed certain cases of eczema to sensitization to common saprophytic molds which grew on the skin lesions.

In a group of fifty-five patients with chronic asthma, the majority of whom had no other positive reactions and eighteen of whom reacted to dust, Flood[12] found five who reacted to fungi by intradermal testing. Balyeat et al.[13] cultured the air in Oklahoma City and found only aspergilli and penicillia. He tested 480 cases by the scratch and intradermal methods and found only four positive reactions. He therefore concluded that molds are of rare importance in allergy.

Jiminez-Diaz et al.[14] made a mycological and clinical study in Spain and concluded that many of the true cases of climatic asthma there are coastal and due to the existence of abundant fungi in the air and in the household articles.

Bernton and Thom[15] report eight cases of vasomotor rhinitis sensitive to fungi.

Feinberg[16] in his criticism upon previous reports on the rôle of fungus in respiratory allergy makes the following remarks: "The majority of reports fail in one or more of the following particulars. There is a tendency to cite only a case or two, emphasizing the rarity of mold allergy. In most instances there is no statement of the number of patients tested among whom the positive reactions were found. In practically none of the previous articles does the author adopt routine use of fungus allergens in his skin tests." In his work, therefore, he adopts routine tests with fungus extracts on allergic patients and draws the following conclusions:

(1) Sensitization to fungi plays an important role, direct or complicating, in the causation of asthma, hyperesthetic rhinitis, and hay fever.

(2) In a series of 243 patients with respiratory allergy, sixty-eight (29 per cent) had positive cutaneous tests to one or more of the fungus extracts enumerated.

(3) The majority of these fungi were the ordinary molds whose air-borne spores form a ready opportunity to cause inhalant allergy.

(4) In a total of 590 patients, consisting chiefly of various forms of respiratory allergy in whom tests with yeasts were made, sixty-five (11 per cent) reacted.

(5) Fungus sensitive patients are usually sensitive to house dust, but patients sensitive to the latter may or may not be sensitive to fungi.

I would include in the above group some of the so-called atopic dermatitis cases which frequently show the presence of respiratory allergy.

Other writers on the subject of mold allergy include Cadham[17] reporting a case of asthma due to grain rusts; Bernton[18] mentioning a case due to *Aspergillus fumigatus;* Cobe[19] a case due to a tomato vine mold, *Cladosporium fulvum;* Credille,[20] a case due to *Aspergillus fumigatus;* and Vaubel,[21] a case due to yeasts growing on plants.

The rôle of fungi in dermatology has been well covered in numerous papers, and repetition is unnecessary. No new clinical varieties have been described since Dr. C. J. White's descriptions in 1919 and 1927.[22, 23]

The biologic investigations have been well reviewed by Dr. Arthur M. Greenwood in his paper on Fungus Diseases of the Skin.[1]

An attempt will be made to discuss briefly the *hematogenous spread of dermatophytes.* The works of Sutter,[24] Bruusgaard,[25] Jessner,[26] Artz and Fuhs,[27] Fried and Segal[28] and others prove that the spread of fungus infection can take place through the hematogenous and lymph routes. Sutter was able to isolate the *Trichophyton granulosum* from the lymph node of a patient with kerion and a lichenoid exanthem. Bruusgaard reports the case of a patient, aged sixty-eight, with a severe kerion of the beard of two months' duration. The temperature was 38 c., and he was prostrated and had pains in the joints and muscles. An injection of trichophyton gave a weak reaction. Within two days of admission he developed a general nodose eruption, the lesions varying in size from one-fourth to one inch. Miliary pus foci developed on the surface of these lesions, and around the older lesions fresh papulopustules appeared. A fresh nodule barely twenty-four hours old was excised and microscopic examination showed bodies like spores, while culture produced a growth of *Trichophyton gypseum,* the same organism as that recovered from the beard. There does not seem to be any reason to doubt that the infection was hematogenous in this case. Jessner obtained a positive blood culture of *Trichophyton gypseum* in a case of tinea barbae. Arzt and Fuhs have obtained a growth of *Microsporon audouini* from the blood of a patient with a microsporon infection of the scalp. Fried and Segal state that Saeves reproduced for the first time cutaneous lesions in a guinea pig infected intracardially with *Trichophyton gypseum* and *Achorion quinckeanum,* while Kogoj was able to reproduce cutaneous dermatoses by injecting emulsions of spores of *Achorion quinckeanum* in the lumbar sac, the subarachnoid spaces, the testicles and the liver. Fried and Segal reproduced cutaneous lesions in the following manner. They used a culture of *Trichophyton gypseum* which was emulsified in salt solution and then filtered. The emulsion was introduced into the marginal vein of the ear of twenty-nine rabbits and positive results were obtained in eleven (38 per cent). The lesions in all animals appeared only in scarified areas of the skin. They explained the localization of the lesions as follows: When introduced into the blood, trichophyton remains in the circulation for a certain period. In instances in which the skin is intact, the normal wall of cutaneous capillaries serves probably as a barrier interfering with their "diapedesis" and, therefore with the ultimate formation of a skin lesion. Shaving, scarification, or any other factor leading to local inflammation favors the migration of the parasite from the papillary capillaries into the skin.

Occupational Dermatoses and Fungi.—The question of the relationship of fungus infection to industrial disability is frequently a difficult one to answer.

In general it is now held that a primary fungus infection is not compensable unless its source can be proved to be a contact in the industrial plant concerned. Of the large number of industrial hazards, only a few are known to

be directly responsible for the causation of a dermatomycosis. Instances where a fungus infection is superimposed upon an industrial dermatosis are more frequent.

Fungi and Internal Medicine.—When fungus diseases are referred to, one immediately thinks of the dermatomycoses and is more or less unaware of the possible damage these pathogenic fungi can do to the viscera. It is true that thus far most of the literature on pathogenic fungi has been written by dermatologists, notably Sabouraud, Jadassohn, Bloch, Castellani, Weidman, Williams, and a good many others, yet one does find scattered reports of diseases of the various organs caused by fungi, particularly those in the yeast-like group. I shall attempt to give a brief summary.

Meningitis Due to Fungi. About thirty-two cases of torula meningitis are thus far reported in literature. Two of these cases have been reported by Stoddard and Cutler[29] in 1916. Blastomycotic infections of the meninges have been recorded, notably by Badham,[30] Swift and Bull,[31] Williams[32] of Australia, and Gaspar[33] in the United States. Hyslop, Neal, Kraus and Hillman[34] described a case of sporotrichosis meningitis and cited about ten cases recorded in the Italian literature, with five others from miscellaneous sources. Cann and Hollis[35] recently reported a case of actinomycotic meningitis in a girl of nine years, and said that Herbert had found reports of twenty-five other cases in the literature, but that they have not been proved culturally. Cases of moniliasis with meningeal involvement have also been reported.

Bronchopulmonary moniliasis has been reported from practically all parts of the world. Castellani described this disease as early as 1912.[36] Numerous other papers have followed, but the number of reported cases in American literature is rather sparse.[37]

The monilia organism may be the primary etiologic agent, but it must be borne in mind that frequently this organism may be a secondary invader in the air passages of individuals infected with some primary bacterial agent.[38, 39, 40, 41] The finding of monilia in the sputum is not sufficient for a diagnosis of bronchopulmonary moniliasis. This condition is usually caused either by direct contact or inhalation, or may result from the extension of oral or cutaneous lesions.

Bronchopulmonary moniliasis has been divided into three clinical types.[38, 42] The classification is based chiefly on the severity of the infection. The mild type is associated with cough and mucopurulent sputum. Examination of the chest in these cases is often negative, but it is not unusual to find a few scattered râles. The clinical course frequently extends over a period of several months, at the end of which time these patients may recover spontaneously or the case may go on to the severe type. The moderate type presents the picture of bronchial catarrh, fever, cough, paroxysmal dyspnea and anemia. In other words, the third type simulates tuberculosis a great deal. Examination of the chest may reveal signs of pleural thickening or consolidation. These cases are frequently fatal.

Both acute and chronic types have been described.[43] In the former the onset is sudden and rapidly terminates fatally. The chronic type is usually slow in its onset and tends to follow a protracted course with frequent remissions and exacerbations; lasting in some instances over a period of ten years.[44]

A discussion on thrush and sprue is omitted since there is a good deal published on these subjects.

Now for a bit of imagination; for after all, imagination has played a great part in scientific discoveries. Therefore the one with imagination and a partiality to mycology asks himself the following questions: "How about bronchiectasis? May it not be due to a fungus, for it does seem to follow a course similar to diseases caused by fungi, i.e., its chronicity and its afebrile or low fever course. Has ulcerative colitis been eliminated from the class of diseases caused by fungi? How about so-called idiopathic splenomegaly?" We are aware of the involvement of the spleen in systemic fungus diseases.

Fungi have been blamed for practically every known disease, but the burden of proof is upon the reporter of these cases. Thus far too many reports of diseases due to fungi without substantiation have found their way into the literature. On the other hand, it is very important to bear in mind the causal relationship of fungi to disease.

Treatment.—I propose to mention the more important facts relative to the treatment of fungus diseases. Since these diseases are contagious and infectious, particularly the dermatomycoses, it is advisable to mention prophylaxis first. The patient must be warned against contact with leather or woolen objects of dress, toilet, and sport. Only boilable material should be worn next to the skin. In the case of tinea capitis the child should wear a boilable cap made of gauze or the top of a stocking under his outer cap.

The following rules are to be observed in the prophylaxis of epidermophytosis.[50]

1. Never walk around on any floor in bare feet. Never wear anyone else's slippers or shoes.

2. Before removing slippers place a towel on the floor of the shower or wear rubber bathing slippers.
3. Place a fresh bath mat or newspaper close by the tub or shower and stand on it when stepping out.
4. Wash the feet at least once a day with soap and water.
5. Dry the feet thoroughly, being careful not to leave any moisture between the toes, using a separate towel for the other parts of the body if there are any signs of infection such as maceration, itching, or burning. Powder the feet lightly, especially between the toes, using any borated (unscented) talcum.

Stockings: Wear light cotton or silk stockings. Change them at least once a day. Never wear woolen stockings.

Shoes: Change shoes at least once a day. Never wear rubber soled shoes or sneakers. Sterilize shoes as follows: soak tissue paper or paper toweling in a solution of formalin. Fill the shoes and slippers completely with the soaked paper. Put the shoes in a box or paper bag, tie with a string and place in a closet for twelve hours. At the end of the twelve hours remove all the paper and place the shoes in the sunshine to air and dry for twenty-four hours.

Bathroom and Shower Bath: As far as possible these rooms should be in a sunny, well-ventilated location, and the floor should be kept scrupulously clean and free of unnecessary moisture. The floor of the shower should be arranged so that the water is not allowed to remain stagnant. The value of the antiseptic foot baths before and after entering the tub has not been proved to be most satisfactory. In fact, in some instances I believe it might prove to be a good breeding place for some fungi.

In the case of the swimming pool, one should use bathing shoes in going to and from the pool.

One cannot emphasize too much the importance of a thorough examination of applicants for admission to public gymnasiums, and so forth, and the exclusion of those showing the minutest evidence of the disease, because they can be carriers.

The results of treatment of fungus infections, particularly of the skin, are not as a whole therapeutic triumphs. The mere fact that there is such a multiplicity of drugs used is proof that none of them represent a real specific treatment. I feel that not until we attain a more complete knowledge of the specific fungus involved and its immunology will there be real therapeutic triumph in this stubborn and troublesome disease. Nevertheless, the following suggestions are valuable.

In systemic fungus infections, in bronchomycosis, in dermatomycosis with an accompanying allergic eruption (id) and in refractory cases of dermatomycosis the use of ethyl iodide inhalations is advised (Swartz, Blumgart, Altschule[45, 46]). Favorable results have also been reported with the intravenous iodine therapy. Large doses of potassium iodide by mouth have also been recommended. My experience has led me to believe that the best results are obtained with ethyl iodide inhalations. However, this may be a case where the results are best in the hands of the originator.

Variable reports are found in literature regarding the value of trichophytin, but my experience supports Dr. Greenwood's contention that it has not been of definite value in the majority of cases. It is possible, however, that the vaccine in greater dilution as suggested by Templeton[47] will give better results. For the past six months I have used at the Massachusetts General Hospital a preparation known as Dermatomycol with rather encouraging results, particularly in onychomycosis. It is too early, however, to evaluate this form of therapy. Dermatomycol is a polyvalent vaccine prepared from equal parts of 300 strains of Trichophyton, Microsporum, Achorion, Endodermophyton and Epidermophyton. This preparation is rather highly recommended by the Brazilian dermatologists.

Autogenous vaccines have been recently used and the results evaluated by Robinson and Grauer.[48] Their report is quite optimistic. I believe that Wise's[49] suggestion is valuable. He states, "By pooling the findings on many patients, employing suitable controls and improved methods, dermatologists could clarify a nebulous terrain and conserve much work and time."

Local Treatment in Dermatomycosis.—1. The acute vesicular type (hands and feet). This type is best treated by soaks and wet dressings, either of saturated boric acid solution, potassium permanganate 1-1000 or weaker, or metaphen 1-3000. In the case of pustulation, the use of boric acid solution soaks followed by the application of the following ointment has proved valuable:

℞

Mercurochrome crystals	gr x
Aquae	m xx
Acidi salicylici	ʒ ss
Petrolati	℥ ss
Lanolini	℥ ss

m

Caution: Do not use irritating preparations as they are apt to set the condition on fire.

2. The subacute and chronic type. These

types are best treated with a sulphur and salicylic ointment, six per cent strength or Whitfield's ointment. One per cent thymol may be added to either of these ointments. The above-mentioned mercurochrome ointment has been used successfully in this type.

In the hyperkeratotic type (particularly found on the plantar aspects) the use of either of the following ointments is recommended:

R		R	
Chrysarobini	gr v-xv	Iodine crystals	gr x
Acidi salicylici	3 ss	KI enough to dissolve the iodine	
Sulphuris praecipitatis	3 ss	Acidi salicylici	gr xv
Petrolati	℥ ss	Petrolati	℥ ss
Lanolini	℥ ss	Lanolini	℥ ss

X-ray in the subacute and chronic cases is of distinct value when used in fractional doses, having in mind its limitations and dangers, but it should not be used in the acute types.

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DISCUSSION

THE CHAIRMAN: This paper is now open to discussion.

DR. ARTHUR GREENWOOD, Boston: I congratulate Dr. Swartz on his handling of a difficult subject. I feel quite sure that it will lend itself to publication very well, and be very useful for a general consideration. I also want to congratulate him on his courage in making dogmatic statements in regard to classifications and things like that. I think doing that is a means of getting the subject into proper form. If you try to teach anyone to know all the exceptions to a subject, to state what it may be or what it may not be, the student gets nothing from it. But, in making dogmatic statements he will discover his exceptions later, and I think more or less dogmatic statements on classification, for instance, or diagnosis of a disease are useful. I am quite sure the mycologists will not agree with him, however.

One other thing I wish Dr. Swartz would do some time, and that is to give us a thorough discourse on his ethyl iodide treatment. I am quite sure it is worth while. I don't think it has ever had a complete exposition of its use in Dr. Swartz's hands.

DR. C. GUY LANE, Boston: Dr. Swartz has correctly said that the diagnosis of fungus infection is made more frequently than formerly. The statistics which are accumulating indicate that among the most frequent diseases the diagnosis of fungus infection is approaching or perhaps surpassing that of eczema.

I should advise in this connection, some little caution in making use of this diagnosis in palmar lesions especially. I think the work of Mitchell, for example, in connection with streptococcal infections, the work of Andrews, and the fact that in many cases of our hand lesions we are unable to find fungus through microscopic examination and culture, make us wonder about these indeterminate things which are called fungus infections. We should try to confirm our diagnosis so far as possible by culture or by microscopic examination.

Dr. Swartz classified his industrial cases in two groups. It seems to me we might carry that distinction just a little bit farther. He spoke of the primary fungus infection. There are very few, extremely few, and I believe we can dispel the possibility of many primary fungus infections occurring in industry. We can visualize it in the handling of wool, perhaps in the wearing of wool-lined gloves, but there are but very few primary fungus infections of occupational origin.

On the other hand I believe that his secondary group of infections, that is, the fungus infections occurring as a complication of the original dermatoses is a much larger group. We see numerous cases, I believe, in whom such complications occur. Then I think there is a third group of fungus infection relating to industry in which fungus infection may be very definitely exaggerated by occupational factors. In some states in which it is allowed, this group of cases exaggerated by work may be compensable. Then a fourth class has been suggested—I haven't yet seen any in this group, but a group has been suggested I think by Cleveland White of Chicago where a previous fungus infection may sensitize the skin to an industrial irritant. I am not sure that this may occur, but there are at least three groups in which there may be a relation to occupation.

THE CHAIRMAN: Are there any other gentlemen who wish to speak? I am sure there will be a great many questions regarding this paper. The point has been raised about fungi in industry, and I wish some of you gentlemen would elaborate that point.

DR. J. HARPER BLAISDELL, Boston: Those of us who are called upon to give medical testimony in industrial cases, I can assure you, are clothed in a miasmic fog of confusion when it comes to the interrelation of fungus disease and industrial dermatitis. The law in this Commonwealth states that a man who receives injury causally related to his employment is entitled to compensation, and I agree with the previous speakers who say that a primary fungus infection of industrial origin is a very rare thing.

The other day I came across this situation: A large industrial plant, in which it was necessary for the workers to change their clothing completely before and after working, provided the men with a shower bath, in other words, club facilities. In that plant at that time there was starting an epidemic of fungus infection of the feet. Does that constitute an industrial dermatitis causally related to employment? That is a question, in that particular instance, which the Courts have yet not decided.

Now, of course, we do see a great many cases of secondary fungus infection following injury and industrial dermatoses, and under the law the workman is entitled to compensation not only for the original industrial dermatitis, but for the secondary complications from the fungus infection which may last many weeks after the original dermatitis.

I call your attention to this situation: It is authoritatively stated that most of us are carrying fungi of some sort about our person. I think it is a fact that an industrial dermatitis, superimposed either upon an occupational fungus infection or a quiescent fungus infection, may result in lighting up a very active fungus dermatitis. But should we take refuge behind that fact that every one of us probably has fungi, and say that in the specific instance this man had an original fungus infection which has been lighted up and therefore we do not expect to be liable from the resulting chronic fungus infection. That is an important medical point because under the law in this State if a man with an original nonindustrial condition acquires an industrial dermatitis which lights up his first nonindustrial condition, he is not entitled to compensation beyond the length of time ordinarily required to take care of the industrial condition. In other words, a man with syphilis, who receives industrial injury which lights up his syphilis, does not receive compensation for the rest of his life for the original syphilis, but only to the extent of taking care of his industrial injury. All of these facts, I think, make for confusion, and it is for us to determine to what extent this situation can be clarified.

THE CHAIRMAN: Any further discussion? If not I will call upon Dr. Swartz to close the discussion.

DR. SWARTZ, Boston: I want to thank those who discussed this paper. Dr. Lane is perfectly correct in adding a third group. I fully agree with him. In answer to Dr. Greenwood's question, I wish to state that I disapprove of rubber-soled shoes because they cause excessive perspiration, which is a good background for fungi.

Under the discussion of the relationship of fungi to internal medicine I did not have the time to cite the following case which I saw at the Massachusetts General Hospital: A woman, aged 45, had an unexplained temperature and complained of excessive pains in the lower extremities. On examination she showed the presence of an enlarged spleen. All laboratory tests, including Widal, were negative. The spinal fluid upon cultural studies did not show the presence of any bacteria. Because she had a chronic paronychia and some dermatosis of the hands, a dermatologist was consulted. Because of the monilia infection of the nails, I felt it wise to study the spinal fluid, blood, and urine for the presence of a similar organism. Both the centrifuged spinal fluid and the urine, when planted on special media, showed the presence of a monilia similar to the one found on the nails. One blood culture was negative. I believe that repeated examinations might have resulted in similar findings.

I was asked to discuss ethyl iodide inhalation therapy. I have already described it in literature, but I shall outline it briefly again. The purpose of ethyl iodide inhalation is to maintain massive concentration of iodine in the blood stream. When using ethyl iodide be sure to get the pure preparation, free from phosphorus, that is, a nontoxic iodine preparation. We have devised a special sort of inhalation apparatus for ethyl iodide. The dosage we use in adults is one and one-half cc. per dose, which is the equivalent of three grams, and increase one-half cc. per dose to three cc. which is equivalent to six grams. In some cases the dose is as high as five cc. or ten grams. It is administered on two successive days, skipping the third day. The number of treatments depends on the condition treated. We have found that infections caused by the yeast

organism require a greater number of treatments than those caused by the ringworm fungi. The only serious complication we had was peripheral neuritis which cleared up in about three weeks after the cessation of the inhalations. Only two such complications occurred in a series of about 500 cases.

(Dr. Joseph Muller of Worcester then presented his paper on "Nevi.")

THE CHAIRMAN: Now, Gentlemen, it gives me the greatest pleasure to introduce to you Dr. Marion B. Sulzberger of New York City, than whom, in his chosen subject of today, there is perhaps no one in these United States who is such an authority upon the subject. We are fortunate indeed in having him with us, particularly as it was primarily announced, as you know, that Dr. Louis Schwartz of New York, of the United States Public Health Service, was to have spoken to us upon "Industrial Dermatoses." Unfortunately Dr. Schwartz fell ill, and is still ill and cannot be here, and Dr. Sulzberger, in answer to my appeal for a pinch-hitter very graciously said, "Why, surely."

We owe him a debt for that too. As I say, I take great pleasure in introducing to you Dr. Sulzberger of New York City, who will speak to you upon "Definitions and Classifications in Dermatologic Allergy."

REMARKS ON DEFINITIONS AND CLASSIFICATION IN CERTAIN FORMS OF DERMATOLOGIC ALLERGY*

BY MARION B. SULZBERGER, M.D.†

IT is most unfortunate that you will not have the opportunity of hearing Dr. Schwartz's excellent paper on Industrial Dermatoses, and that you will have to accept my rambling and unprepared discussion in its place. However, when, only a few days ago, your chairman, Dr. Towle was kind enough to ask me to substitute for Dr. Schwartz, he assigned my subject, and I told him that I would attempt to fill in to the best of my ability.

I would like to begin with the most difficult portion of this subject,—and that is, a discussion of the definition of the word "allergy". There are certainly many authors, even so-called experts in the field, who both in speech and writing use this term either loosely or, in some specific and exact but private manner, without defining the exact limits and boundaries of their own individual concept. I believe that both of these practices have led to confusion.

I shall, therefore, preface my remarks with the definition of "allergy" as first formulated by v. Pirquet; as first employed by Schick; and as generally accepted by immunologists today; and state that I, too, have accepted and always employed the term in its original and classic sense. For to my knowledge no better and no more exact definition is available; and it is my belief that here, as elsewhere in scientific terminology, any radical modification in a concept demands the coining of a new term.

According to v. Pirquet (1906), allergy designates any *acquired, specific* alteration in the capacity of an organism to react.

This alteration must be produced by a previous exposure or exposures in order to fulfill the requirement of being "acquired". And the alteration must be made manifest by subsequent exposure to the same or to immunologically related substances, in order to fulfill the requirement of being "specific".

You will note that this definition is extremely wide. It includes all acquired, specifically altered, reactions, regardless of the mechanism by which this alteration is produced, regardless of the substance (living or nonliving agents) which produces the alteration, and regardless of the nature of the alteration elicited (quantitative alterations—that is, alterations in the direction of hyperergy or hypersensitivity, of hypoergy, or of anergy and immunity are all thus included under allergy).

I should like to stress at this point that no mention is made of antibodies and that in this, the original concept of allergy, the demonstration of antibodies is not by any means an obligatory requirement for the inclusion of a specific alteration within this category of phenomena. Indeed, the vast majority of specifically acquired and classic allergic alterations of reaction seen in human beings are not accompanied by the formation of antibodies demonstrable by any known present methods or technics.

In dermatology there are found many of the most clear-cut examples of such specific alterations in the capacity to react. A large number of these are indeed among the original examples of allergy mentioned by v. Pirquet. I need remind you only of the altered reactions to vaccinia which appear on revaccination or after smallpox, the altered reactions to tuberculin which appear after tuberculous infection, and the altered reaction to diphtheria toxin as made manifest in the negative Schick test.

However, not only in these specifically acquired alterations in infectious processes, but more particularly in reactions to nonliving agents, the study of skin phenomena has yielded the most important contributions to basic

*Read at the Annual Meeting of the Massachusetts Medical Society, Section of Dermatology and Syphilology, Springfield, June 8, 1936.

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principles in the field of allergy. There are no more clear-cut examples of acquired and specific hypersensitivities than those which occur in the eczematous or contact type of hypersensitivity acquired by exposure to simple chemical substances. For here, in contrast to the hypersensitivities in such conditions as hay fever and asthma, adequate experimental proof has been brought both that the skin hypersensitivity has been acquired and that it is specific. I refer here to the experimental sensitization of the human skin with primrose (Bloch), with mercury and formaldehyde (Haxthausen), with orthoform (Schwarzschild), with mesotan (Silverberg), with paraphenylendiamin (R. L. Mayer), and innumerable other experimental sensitizations of this type.

In the studies of such eczematous sensitizations to simple compounds, and in studies of drug eruptions, both of the fixed and of other types, dermatology has contributed toward a clarification of some of the most important principles in the modern concept of allergy. One of these points deals with the fact that the shock tissue which enters into the reaction may be sharply limited and may embrace certain circumscribed portions of an organ, while other parts of the organ remain "immune" and do not participate in the allergic response. This is well illustrated in the so-called fixed drug eruptions in which one or more circumscribed areas of the skin may react in a most violent manner, while other areas remain without demonstrable reaction. The sometimes isolated and circumscribed power to react which may be confined to a specific part of an organ is further evidenced by the division of skin reactions into eczematous responses and responses of urticarial type.

Because of the importance of these two particular forms of dermatologic allergy, I should like to confine the remainder of my remarks to these two types of responses.

EPIDERMAL REACTIONS

It is today granted by the vast majority of careful students of this problem that in the eczematous or so-called contact type of hypersensitivity, the epidermis itself is in all probability the primary shock tissue. The response at any rate is *primarily* epidermal, and the vascular reaction in the upper cutis, while almost always present, is in all probability an accompanying or secondary phenomenon.

I believe that this recognition of the epidermis (epithelium!) as a shock tissue is of an importance far beyond its practical significance in dermatology. However, it must be granted that it has not yet been proved with absolute certainty that the epidermis alone is actually the sole site of hypersensitivity in eczematous responses, and while the mass of evidence certainly points in this direction, the problem merits further study.

Nevertheless, the concept of an *epidermal* shock tissue proves of great heuristic value. For, from this premise alone may be deduced many of the outstanding characteristics of eczematous hypersensitivity:

First: The characteristic of the reaction time; that is, the time elapsing between the exposure of the hypersensitive epidermis to the specific allergen and the first appearance of the clinical manifestations of hypersensitivity. In the case of eczematous responses, as is well known, a period of hours to days elapses before the dermatitis appears. This response is remarkably slow compared, for instance, with the explosive, immediate types of reaction seen in vascular, urticarial hypersensitivities.

But the slow development of this reaction becomes comprehensible when we realize that the epidermis possesses no blood vessels, that is, includes no structures capable of almost immediate alterations in permeability or of speedy contraction and dilatation. In the epidermis, therefore, the damage produced by the allergen must manifest itself slowly, with gradually increasing edema and eventually with the formation of the characteristic spongiosis and intraepidermal vesiculation.

Secondly: If the epidermis is the shock tissue in eczematous responses, it must be evident that those substances which can reach this tissue unchanged and in the highest possible concentration, will almost inevitably be those which are most likely to sensitize and to produce the reactions of hypersensitivity. It is obvious, therefore, that substances coming from the outside world, which reach the epidermis by external, contact exposure, will prove to be the most common eczematogenous noxae. For these agents will not have to undergo denaturization, they will not have to be diluted by the blood stream, and they will not be prevented from reaching the epidermis by the usual, normal, relative impermeability of the vascular walls.

Thirdly: It is to be recognized that the living cells of the epidermis which constitute its only possible shock tissue are normally protected from external contacts by natural barriers. These barriers are of both physical and chemical nature. The two most important are undoubtedly the nonliving, horny protective covering of the stratum corneum and the fatty, water-repellent, sebaceous film which covers the normal skin surface. In addition to these two barriers, the healthy skin possesses the ability to neutralize both acids and alkalis.

(I should like to state here in parentheses that I believe that minute but abnormal alterations in any of these protective mechanisms are in all probability of almost incalculable importance in predisposing to a state of susceptibil-

ity to epidermal sensitization. If this is true, it is most apparent that a study of the underlying constitutional or local factors which are capable of producing abnormalities of cornification, of the secretion of sebum, or of the acid-alkali neutralizing powers of the skin surface will undoubtedly tend to lead to an understanding of at least some of the factors which determine the mysterious, and often sudden, appearance of eczematous hypersensitivity.)

Assuming the epidermis to be the shock-tissue, from the mere consideration of the nature of the normal protective forces which shield the living epidermal cells, we may logically conclude the nature of many of those substances which will be most likely to produce eczematous hypersensitivity.

Keratolytics and substances possessing a capacity to precipitate, cleave, shrink or otherwise damage the horny layer will be capable of either themselves sensitizing or of preparing the way for sensitization by other substances. Caustics and alkalis (soaps, and so forth), acids, such as picric acid, formalin and similar agents belong to this group.

A second category embraces those substances which are either fat solvents or are themselves prone to enter into solution in fats, lipoids and oils. Here included are the many different forms of fat and lipoid solvents and detergents, and above all, the oil fractions of plants (ragweed oil, poison-ivy oil and numerous other resins and oleoresins) and the animal fats (lanolin, and so forth).

In addition to these keratolytics and fat solvents and fatty substances, another group is presumably able to pass the natural barriers which protect the living epidermis. This group comprises ionizable chemicals of small molecular dimensions. The metal ions such as mercury, nickel and arsenic are common examples of this group.

There is a fourth group of substances which is obviously capable of coming readily into contact with the living epidermal cells and which therefore can be considered as potential allergic eczematogenous agents. This group comprises those substances which become fixed to the horny covering or which have a marked affinity for ectodermal structures. I would here include, first, the dyes which by their very nature form fast combinations with horny matter (paraphenylendiamin, azo-dyes of all kinds, and so forth), and also the local anesthetics (novocain, butyn, butesin, and so forth) with their well-known affinities for ectodermal tissue.

A fourth characteristic which becomes self-evident when one considers the epidermis as the shock tissue in eczematous, contact type sensitizations, is the indicated form of skin test. In order to bring to light epidermal hypersensitivity, it is of course necessary to use that method of testing which will permit the most intimate contact of the allergen with the shock tissue concerned. Obviously, neither scratch tests nor intracutaneous injections serve this purpose. For both of these methods force the allergen through the epidermis and into the rapidly moving fluid currents of the superficial cutis, which carry away the bulk of the material, and thus prevent the necessary intimate and prolonged contact with the epidermal cells. The patch test must here be employed, for with this test the mechanism which has produced the clinical reaction may be approximated to some degree. The substance is applied to the skin surface and allowed to pass slowly through the protective coverings and to reach the hypersensitive epidermal cells.

As I have before stated, the response in eczematous hypersensitivity is a slow one and this makes it necessary to read the results of patch tests after twenty-four hour, forty-eight hour, or even longer periods have elapsed. The response usually reaches its maximum by forty-eight hours, but in some few cases several days may elapse.

I realize only too well that many of my statements in this connection are as yet unproved, and I submit all of the above, not as a dogmatic statement of facts, but rather as an attempt at clarification and the presentation of working hypotheses. I believe that experimentation may be based upon attempts to verify or disprove many of my statements, and that this line of approach cannot fail to produce results, not only of theoretic but also of practical interest.

For example, if the above considerations are correct, individuals with dry skins, lacking in the normal sebaceous covering, should prove more susceptible to eczematous sensitization with water-soluble substances and relatively immune to fatty excitants; while those individuals with excessively greasy skins would be more protected against water and soluble allergens and more likely to be candidates for sensitization to fat solvents and oil, fat and lipoid soluble allergens.

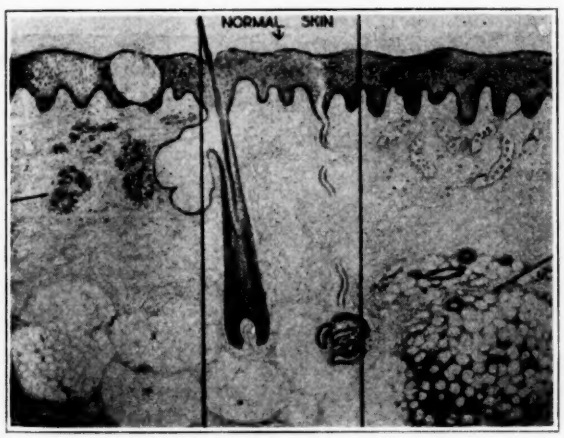
An experimental study of this question is indicated, for if the supposition should prove correct, this would undoubtedly be of practical value. To point out only one possible application, it may be mentioned that workers with seborrheic skins could be chosen for processes involving exposure to water-soluble eczematogenous substances, while those with hyperkeratotic skins could be placed at work in which oily substances constitute the occupational hazard. Moreover, those individuals with an adequate capacity to neutralize alkali at the skin surface could be selected for employment in such oc-

cupations as nickel plating, laundering and so forth. (An interesting study with bearing on this point has recently been reported by Burckhardt from the Dermatologic Clinic in Zurich.)

The various other possible approaches to this complex problem which are obviously contained in the viewpoint I have advanced are too numerous even for mention here.

I must make haste to emphasize that such simple explanations for variations of susceptibility to eczematous sensitization must not of course be considered as the answer to the question of why certain individuals at certain times become sensitized, while others under the same conditions of exposure remain immune. My considerations have embraced only the simple and obvious local interferences with the normal protective mechanisms at the skin surface. While these must be of great practical importance, such alterations in local protection surely cannot fully explain the underlying fundamental immunologic factors which produce in one individual an almost incredible degree of susceptibility to eczematous hypersensitivity, and in another individual an almost complete immunity to this type of sensitization.

A SCHEMATIC PRESENTATION OF THE COMMONER ALLERGIC SKIN REACTIONS BASED UPON (*A*) *HISTOLOGIC LOCALIZATION* AND (*B*) *TIME* REQUIRED FOR THEIR DEVELOPMENT.



Reprinted from J. A. M. A., **104**:1489, 1935—Sulzberger, Wise and Wolf.

I. ECZEMATOUS REACTIONS
1. Site of shock tissue: epidermis
2. Reaction time: 24 or more hours
3. Characteristic lesion: spongiosis and intradermal vesicle
4. Causative substances: frequently simple chemicals or products of fungi
5. Type of test: patch test

II. TUBERCULIN-TRICHOPHYTIN-TYPE REACTIONS
(Not Infrequently Combined With Eczematous Responses)
1. Shock tissue: upper cutis, cutis
2. Reaction time: 24-48 or more hours
3. Characteristic lesion: lymphocyte and later epithelioid cell infiltration
4. Causative substances: usually micro-organisms, bacterial or fungus products (allergy of infection)
5. Test: intracutaneous (48 hours)

III. URTICARIAL REACTIONS
1. Shock tissue: upper cutis (blood vessels)
2. Reaction time: 10 to 30 minutes
3. Characteristic lesion: edema, extravasation of fluid and eosinophiles (wheal)
4. Causative substances: foods, inhalants, products of micro-organisms
5. Test: intracutaneous, scratch or indirect (immediate wheal and flare)

IV. MISCELLANEOUS REACTIONS
(Drug Eruptions, "IDS", and so forth)
1. Shock tissue: deep cutis, cutis, epidermis, follicles.
2. Time: minutes to days
3. Lesions: (a) nodules, (b) fixed areas, (c) multiform dermatoses and follicular lesions, and so forth
4. Substances: drugs, micro-organisms
5. Test: usually inconclusive; sometimes the patch, Moro or intradermal test is of value.

Before leaving the group of eczematous sensitizations, I may mention that sensitizations to fungous products, when evidenced by eczematous or dyshidrotiform reactions, are in all probability to be included in this category. And here again, the premise that the epidermis is the shock tissue permits us to recognize the pathogenesis of eczematous hypersensitivity to fungi. The fungi which produce eczematous responses cannot, as a rule, multiply in living tissues (W. Jadassohn and the author) and are therefore confined to the nonliving media of the horny layer, the nails and the hair. When the products which emanate from these fungous cultures in the horny layer pass downwards, they first reach and thus first sensitize the epidermal cells.

Consideration of this process may serve to explain the intertriginous sites of many fungous affections. For in these areas the macerated and nonliving débris forms a medium for the multiplication of the fungi and for the ensuing production of amounts of fungous allergen which eventually "break down the resistance" and produce the reactions of hypersensitivity.

In a like manner, all influences which tend to the production of hyperhidrosis (nervous upsets, excitement, sports, tight or ill-fitting footwear, and so forth), or to increased accumulation of moisture on the feet in the interdigital spaces (swimming pools, improper drying, and so forth), will lead to an increase of nonliving material as soil for fungi and will thus tend to produce attacks or exacerbations of dermatophytosis and dermatophytids.

VASCULAR REACTIONS

The second group of important skin allergies has characteristics which are in most ways in sharp contrast to the eczematous hypersensitivities just discussed. This second group includes the so-called urticarial or "wheal" and "flare" reactions. The important representative of this type of skin allergies is not, in my opinion, one of the true urticarias; for I believe that the disease known as urticaria, and particularly the chronic form, has not in the ma-

jority of cases been proved to be actually based upon an acquired, specific alteration in response, that is, upon an allergic mechanism.

I believe, however, that that form of dermatosis which has been called neurodermatitis disseminata, pruritus with lichenification, prurigo diathésique, and by many other names, and which we have now agreed to call *atopic dermatitis*, is based upon a submanifest, subclinical, wheal type of reaction; and it is to this dermatosis and to the skin tests elicited in this dermatosis that the following remarks are intended to apply.

As is well known, atopic dermatitis is associated both in the individual and in his family, with asthma, with hay fever and with a certain form of infantile eczema which is best designated as an "atopic dermatitis of the infant". If this disease is, as many observers believe, essentially due to a specific hypersensitivity, it is certain that this hypersensitivity is fundamentally and intrinsically different from that found in the truly eczematous or contact-type dermatitis. For here, the shock tissue is certainly not the epidermis, but is the uppermost vascular layer of the cutis.

Here again the mere consideration of the site and nature of the shock tissue leads inevitably to conclusions regarding the clinical and histologic characteristics of the dermatosis, the nature of the causal allergens, and the type of skin test which must be employed.

In this form of hypersensitivity the blood vessel wall is the shock tissue. Thus, obviously, those substances which can be borne by the blood stream are those most likely to reach the shock tissue in sufficient concentration. (In exceptional instances, and perhaps in infantile eczema even as a rule, *substances may be able to pass through the epidermis* and elicit reactions in the superficial cutis vessels—*transepidermal penetration*).

Since the hematogenous route is the usual one in the clinical production of this vascular reaction, a certain group of substances is immediately suggested as a common cause of this form of cutaneous allergy. Only allergens which are on the whole compatible with the blood fluids are likely to be carried as more or less usual constituents of the blood stream. The allergens in this group are therefore likely to be water soluble, and very often the so-called protein fractions. They usually emanate from ingested foods or from the inhalation of environmental allergens and their subsequent absorption and hematogenous distribution.

It will be seen that this group of allergens corresponds to a high degree to those excitants which produce hay fever, asthma and vasomotor rhinitis. And just as it is probable that asthma and vasomotor rhinitis can be caused by the products of micro-organisms emanating from some distant and often hidden focus, so it is also probable that atopic dermatitis may, in some instances, be based upon such excitants.

I shall not here enter into a discussion of the relative importance of the various nonallergic factors in the production of the itching and of the skin manifestations of atopic dermatitis. I have elsewhere discussed the possible influence of neurogenic and psychogenic factors, and of other constitutional or systemic influences (vasomotor instability, endocrinopathy, and so forth). Suffice it to say that, while it may vary within wide limits from case to case, the influence of these nonallergic factors is often apparent. But it must be stressed that the demonstration of even marked effects of such systemic influences in no way refutes the evidence for the essentially allergic nature of this dermatosis. For it is well known that allergic manifestations of the most typical and characteristic kind are susceptible to the influences of the psyche, the nerves, the blood vessels, the hormones, and of a host of other systemic factors.

The consideration of the vascular site of the hypersensitivity in atopic dermatitis helps us to understand the frequent association of positive, specific skin tests manifested as wheal and flare reactions which are so often found in asthmas and particularly in hay fever. For these two last-named diseases are also primarily vascular reactions, in which a different part of the vascular tree is the site of the shock. The pathogenesis of asthma and hay fever is closely akin to that of whealing: in all three, the superficial blood vessels are hypersensitive, and the contact with the specific excitant increases their permeability and produces extravasation of fluid and of certain cells (eosinophils). In the lungs, this phenomenon is followed by contraction of the bronchioles, and by the other manifestations of asthma; in the conjunctiva and the nasal mucosa, by epiphora, rhinorrhea, and the other manifestations of hay fever; and in the skin, where the fluid cannot escape but remains confined by the overlying, impermeable epidermis, whealing—either clinically apparent or subclinical—is the immediate result.

It is my concept that atopic dermatitis—whether it be in the infant, the child, or the adult—is due to subclinical whealing; and that this subclinical whealing and the accompanying pruritus eventually lead to the epidermal involvement, and to the eczematoid and lichenified appearance. I believe that in infants the epidermis is less impermeable, both from within and from without; and that we therefore see not only transepidermal penetration of allergens, but also transepidermal penetration of extravasated fluids, with the resultant weeping, oozing, crusting, and even spongiosis and vesiculation. (In contrast to the infantile form in the childhood and adult types of atopic der-

matitis, the eruption is dry; and, as is well known, spongiosis and vesiculation are consistently absent.)

I may say, therefore, that I conceive of atopic dermatitis as primarily a subclinical urticarial reaction; and that the epidermal changes are, in my opinion, secondary in nature. This stands in sharp contrast to the eczematous contact hypersensitivities, in which it is probable that the epidermis is first involved and the vascular changes are secondary.

The fact that the blood vessels are the shock tissue in wheal-type reactions indicates not only, as before stated, the nature of the responsible allergens, but also the time which may be expected to elapse between the exposure of the shock tissue to its specific allergen and the first appearance of the clinical manifestations. Here the blood vessels, with their capacity for speedy contraction, dilation, and change in permeability, constitute the shock tissue; and here, therefore, the time required for the reaction to develop will be only a question of minutes. The wheal and flare reaction in the skin is called the "immediate" reaction. This reaction is acute and explosive, just as in the attack of asthma or of hay fever.

Furthermore, in this form of hypersensitivity, we must again employ a test which brings the causal allergens into immediate contact with the shock tissue. For this purpose, we must impel the causal and so-called "protein" allergens (derived from foods and inhalants) through the epidermis, and place them in the vascular layers of the superficial cutis. Either the scratch test or intracutaneous injection is the adequate and correct method.

Since the most experienced allergists disagree as to which of these two means of testing is preferable, it may be stated that, for dermatologists and for all not confining their practice to allergy, the scratch test should be the method of choice. It obviates the necessity for expensive and perishable paraphernalia, for keeping hundreds of separate syringes (to avoid the element of syringe contamination). It does away with the necessity for sterile solutions and technic. And, above all, it obviates, to a great degree, the dangers of systemic and, in some cases, even of fatal reactions.

Perhaps I have unwittingly created the impression that all cases of atopic dermatitis can be cured by immunologic measures alone. This is far from my intention and far from the truth. There are, in my opinion, many as yet unknown factors in the pathogenesis of this dermatosis.

While in my material the identification and elimination of the proper allergens have brought about striking improvement in some cases, in many others the most rigid exclusion of suspected excitants has proved of no avail. In my experience it is the rule that the younger the patient (infants included), the greater the likelihood of the success of allergen elimination. Moreover, it may be stated in general that the younger the patient, the greater the rôle of foods; while the older the individual, the more polyvalent the hypersensitivity, the more prominent will be the part of environmental and inhalant excitants (L. W. Hill and the author). This is perhaps one factor which makes the management of the older cases more difficult.

From the immunologic side, the best we can do today in the practical treatment of atopic dermatitis is to try to eliminate all the known common causal excitants. The patient's room, for example, should contain no needless dust producers (pillows, mattresses, overstuffed furniture, and so forth), and no dust catchers (drapes, carpets, rugs, and so forth). The safest bedding is sterilized horse-hair (even for those sensitive to horse dander!). Silk, feathers, kapok, and orris root have been shown to be particularly active allergens in atopic dermatitis. Among the foods, not one is above suspicion. But the most common offenders, as is well known, include eggs, wheat, milk, and fish. I believe that chocolate (cocoa) may be added to this list.

Such elimination measures, plus the judicious use of x-ray, and particularly when combined with the art of selecting the topical remedies best suited to the individual case, promise to give the best results. Systemic measures (including thyroid extract, cortical extract, arsenic, bromides, calcium, vitamines) seem to benefit some cases. And it is certain that the psychic and nervous state, if abnormal, merits attention; and that foci of infection (fungi, streptococci, staphylococci) must be sought and if possible eliminated.

In otherwise hopeless cases, hospitalization or other change of environment often produces abrupt and almost miraculous improvement. The cause of this striking influence of environment (clearly to be seen in infantile, and childhood, as well as in adult, atopic dermatitis) may ultimately lead to a better understanding of the possible importance of as yet unrecognized environmental allergens (house-dust ? fungi ?).

I know that if I do not volunteer the information I shall be asked concerning specific hyposensitization treatment. In my hands this has proved useless in all those cases of unquestionable atopic dermatitis, in which I have been able to give the usual measures a fair trial.

This is in sharp contrast to my success with specific hyposensitization in contact dermatitis due to pollen and plant oils (ragweed and ivy oil, tulip oil, and chrysanthemum oil).

I am not surprised at this failure of present methods of specific hyposensitization in atopic dermatitis. For, similarly, it is apparently extremely difficult to reduce the wheal-type hypersensitivity of the skin by present methods. This is brought home strongly by the observation of the persistence of wheal reactions of the skin, even in patients who have received hundreds of injections for the control of hay fever or asthma; and, surprisingly enough, the wheal skin reaction often persists in spite of the successful clinical desensitization of the mucous membranes and in spite of complete clinical relief.

As I have stated above, I have come to consider the manifestations of atopic dermatitis to be based upon a type of subclinical whealing. And since it has been shown that wheal-type reactions of the skin cannot, as a rule, be materially reduced by present hyposensitization measures, I cannot find it astonishing that these same hyposensitization measures have, thus far, met with little or no success in what I hold to be the analogous whealing of atopic dermatitis.

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I regret that time does not permit me to consider here the manifestations and problems of acquired, specific alterations of the skin in infections, in drug eruptions, and in other processes. However, I hope that some day I shall be permitted to discuss before this Society these other forms of skin allergy.

CHAIRMAN TOWLE: Our next paper is by Dr. Edward C. Sullivan of Springfield. Dr. Sullivan.

THE DOCTOR AND EARLY SYPHILIS*

BY EDWARD COPPINGER SULLIVAN, M.D.†

THIS paper is rather elementary in its scope, but at times it is well to get down to fundamentals and review what we know, what we should know, what advances have been made in some particular field, and analyze our mistakes of the past in order that we may more ably conduct ourselves in the future. It is addressed especially to three classes of erroneous thinkers: those doctors who believe that when the objective symptoms disappear under a little treatment the patient is cured; those who believe it is a hopeless situation at the best, so what is the use; and those who believe that their clientele is so fine, or refined, and syphilis such a rare disease there could be none of it among them.

A good many years ago Dr. Osler said that we would be better doctors if we took down our impressive Latin diplomas which none of us could read anyway, and put in their place in large letters this admonition: "Never forget that there are two diseases, tuberculosis and syphilis." Judging by the record that has been made in the control of tuberculosis in Massachusetts in the past thirty-five years, someone must have taken heed of the first part of that advice as that disease has been reduced to about twenty-five per cent of what it was in the year 1900. There has also been a glorious record made by the medical profession in the control and practical elimination of typhoid and diphtheria.

By contrast, the record of syphilis offers a sad commentary of sloppy thinking, "pussyfooting" and general ineffectualness on our part as it still ran on like the babbling brook, unrestrained, until most recently. If we take into account the difference in the communicability of tuberculosis, diphtheria and typhoid, as compared with syphilis, there must be some answer as to why the latter has thrived all these years. There is an answer and a large proportion of it is a quite simple one and may be summed up in lack of education of the public, and lack of education of the doctors.

The United States Public Health Service makes a conservative estimate that there are 425,000 fresh infections with syphilis yearly. Measles is the only reportable disease that leads it. Syphilis is rated among the first four of the killing diseases, but in the meantime it leaves a trail of suffering, misery and disaster, not only among the guilty, but also among the innocent victims who represent approximately forty per cent of the infected. One hundred times as many children died in Massachusetts of congenital lues in the past ten years as died of infantile paralysis. We are paying a big price to entertain this unwelcome guest.

Syphilis is not a rare disease by any means and also let me try to impress upon you that the *Treponema pallida* is not a respecter of high social or financial position, but that syphilis runs fairly evenly through all the strata of society proportionately. There is no one here who has not seen all too many of the tragedies of late syphilis, which in the light of our present-day knowledge of the treatment of syphilis, should become almost a thing of the past. There is a woeful dearth of information of the truth about syphilis on the part of the public, but we must also admit that the doctors have not been wholly without fault. In fact, Dr. John H. Stokes frankly accuses the doctors of being

*Read at the Annual Meeting of the Massachusetts Medical Society, Section of Dermatology and Syphilology, Springfield, June 8, 1936.

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the chief offenders. We must leave the function of the education of the public in matters of sex hygiene to the proper organizations, but we have no alibi at all for the rôle we are playing, or rather not playing, as individuals toward the control of this greatest scourge of mankind.

When we consider what has been done in the control of tuberculosis, it is astonishing that so little has been done about syphilis. There is no serious disease in which adequate treatment presents more striking results. There is no field in preventive medicine which offers greater hope for the practical eradication of a disease in a single generation, and there is no field in which less is being accomplished. Some of this fault must be placed on our shoulders and, if we are to retain our place in the public esteem, we must exert ourselves to bring about a better understanding of syphilis and be leaders in the dissemination of that knowledge rather than to procrastinate further and eventually find ourselves in the untenable position where the public knows more than we do; and the public is becoming eager for that knowledge. A few months ago a New York paper was the first newspaper in the United States to publish a series of articles on syphilis. It took courage on the part of the editorial department not to "offend" the readers of this periodical. The demand was so great that reprints were later printed in pamphlet form and of these hundreds of thousands have been sold. Apparently the public is not so easily "offended" as the publishers have formerly thought.

Let us take stock of our mistakes of the past. The first is errors of early diagnosis. The average doctor is apt to regard the genital sore all too casually and make an "eye diagnosis" that it is nothing, or a chancre. Either one is eminently unfair to the patient. If it is syphilis, the patient needs a lot of treatment, and if not, it is unjustifiable to place the patient in the position of taking the treatment for syphilis, not to mention that you have placed the stigma of syphilis in his mind forever. The days of "guessing" what the genital lesions are, have gone by. All genital sores should be regarded as possibly luetic until it is proved that they are not. The old textbooks have beautiful pictures of the various types of chancres and elaborate descriptions on how to differentiate them and the nonluetic lesions, but not the keenest diagnostician of the past can compare with the modern dark field examination. The diagnostician was frankly making a guess and had to await the appearance of the secondary manifestations to clinch his diagnosis while the dark field is an accurate and rapid method. "Guessing" is as antiquated as kicking your tires to estimate the pressure.

The dark field is a fairly simple procedure in the hands of one trained to its use and an exact diagnosis can be made in a few minutes. If the treponema is present in the lesion it can usually be found the very first day. Waiting for a Wassermann is never a substitute for the dark field as there is too much valuable time wasted. The most important thing from the patient's standpoint is to have a diagnosis made at once and adequate treatment started in the seronegative stage, as then he has almost one hundred per cent chance of cure. From the appearance of the chancre to the time the luetic is put under treatment is the most important period of his life, so far as his future health is concerned. If he reports to you early, why not give him that opportunity to safeguard that health and not throw away a lot of his chances by ducking the issue. This is said with due regard to the general opinion that the patient with secondary signs or symptoms has a better chance than the patient put under treatment in the so-called seropositive primary stage.

Also let me implore you not to put any mercurial on a lesion if you are going to refer the patient for a dark field examination. The treponema cannot be found in the lesion for from twenty-four to forty-eight hours after a mercurial is applied. The mercury has no beneficial effect on the lesion and you are forcing the operator to the trouble of getting his secretion for examination from the inguinal glands. A chancre *per se* is not a disease, it is only a symptom that the patient has a general infection with syphilis.

I wish particularly to stress the fact that we do not inspect our cases of gonorrhea with enough thoroughness. We see quite a number of cases of late syphilis in which there is no history of chancre but only one of gonorrhea, and I mean in patients who are doing their best to be truthful and co-operative. Every case of gonorrhea follows an exposure that has also the potentialities of infection with syphilis. There must be a not inconsiderable number of cases of gonorrhea in which the luetic infection takes place at the same time and is unobserved. If one would be on the alert for the intra-urethral chancre and not lightly dismiss slight lesions of the glans penis and coronal sulcus in gonorrhea, there would be more cases of syphilis discovered early instead of late. I believe that all patients with gonorrhea should have a Wassermann done before dismissal, and what I truly believe to be better routine is that they should have a Wassermann at the first visit as well. Then if the later Wassermann is positive, you know whether you are dealing with an early or late syphilis which is not always so easy to differentiate in asymptomatic syphilis.

Cases of chancroid, which by the way are not common in this section of the country, after repeated negative dark fields, should have a

series of Wassermanns over a period of four months as it is not rare to have an infection with the treponema as well as Ducrey's bacillus.

In the past fifteen years there has been an increase in the number of extragenital chancres, and here again the doctor is not of a sufficiently suspicious frame of mind. The "cold sore" on the lip which is not typical, is indurated, and shows no signs of healing should be regarded with suspicion. Sores inside the mouth, on or beneath the tongue, or on the tonsils, attended with cervical adenopathy should in many cases be regarded with the greatest suspicion, especially in young people, and resort had to the dark field. The dark field may be done on secretions obtained from the lesions themselves where there is always the difficulty of differentiating the treponema and similar organisms, although most mouth lesions have existed so long that the Wassermann is usually positive and hence a check on error, or what is better, is to take secretions from the cervical glands where the treponema would be the only spirochete present. Many a blunder will be averted if these lesions are not too lightly regarded, and some palliative mouthwash prescribed, only to find yourself deeply chagrined when the patient later develops a distinctive efflorescence of secondary syphilis. Any pharyngitis or laryngitis which persists for several weeks is waving the red flag and begging for a Wassermann.

The primary lesions of the fingers, hands, cheeks, eyelids, and so forth, should in most cases arouse suspicion long before they do. Any sluggish ulcer that is painless, indurated, has no signs of sepsis surrounding it and shows no signs of healing, should give pause for thought that there is such a disease as syphilis. Always look for adenopathy in the satellite glands in suspected extragenital lesions. It is well to remember that only about seventy per cent of syphilis develop a noticeable secondary eruption.

Another unrecognized origin of the late syphilis we see in patients with no exposure of their own, and a proved uninfected family, is undiagnosed syphilis contracted when they were babies or children. There is the possibility that it was kissed onto them by some adoring, but infected, relative or family friend. I would suggest a search for a possible primary lesion and adenopathy in skin eruptions of undetermined nature or in supposed exanthemata in which the skin lesions persist beyond the usual time.

Now let us review the common errors committed in the treatment of early syphilis. If you will form a mental picture, that in a broad sense, the lesions of early syphilis are inflammatory in character while the lesions of late syphilis are truly destructive in character, there can be no argument as to when is the best time to accomplish results of a permanent nature. There is no easy road to the cure of syphilis, but it would be impossible to overemphasize the point that it is early, and adequate, and continuous treatment, over a long period, that gives the only chance for the looked-for cure.

The patient that is given five or six, or even twelve, injections of an arsenical with the consequent disappearance of the symptoms, and perhaps unfortunately a negative Wassermann, and then patted on the back and assured he is all right and need never worry again, has not received medical service. On the contrary, he has been done a grave injury. I will admit that in the very rare case he may be cured, but it is highly improbable. There are no good, but several bad effects in store for him and his. That patient has been lulled into a sense of false security. There has been turned loose on the community a potential broadcaster of syphilis and the prospective parent of a syphilitic child. That patient will almost surely have a relapse and become infectious again, or later on, some doctor is going to have the problem of trying to patch up a case of late syphilis which result is about as permanent as an adhesive tape repair job. The patient had his chance but it was thrown away.

In the past fifteen years we have had enough experience to establish quite definite criteria as to how much, and how long, the early case of syphilis should be treated. I am speaking in terms of probable ultimate cure and not about sufficient treatment to guard only against later mucocutaneous relapse. The early luetic should receive from thirty to forty injections of an arsenical, and from sixty to one hundred doses of heavy metal, preferably bismuth. This treatment will last from one and one-half to two years, and it is important that this treatment be given without any rest periods. There are several different schemes of alternate arsenic and bismuth, or simultaneous treatment with both and follow-up with bismuth until the required amount is given, but whatever scheme is used there should be no rest periods. It is during the rest periods that the infection has a chance to gather strength again. It is good therapy to give three injections of arsenic the first week.

A Wassermann should be made monthly, and if it remains persistently positive after a few months, in all probability you are dealing with central nervous system involvement and appropriate measures should be taken. It is not common to find central nervous system syphilis in the face of a negative Hinton test which

is the one used in this state. It is the continuous pounding away with treatment within the limits of the patient's tolerance that offers the best possibility of curing the disease. Let me interpolate at this point that a human being as well as a disease is being treated. There are no half-way measures that are of any use and there is no substitute for arsenic in rendering the patient noninfectious early and in the ultimate cure. It makes little difference what brand of arsenical you use or what preparation of bismuth, even though the salesman assures you that his house makes the best, and subtly, or not too subtly, infers that you must be a congenital idiot if you do not use his. I repeat, it is the amount of steady, regular, persistent treatment that counts. After the period of treatment is finished, the patient should be kept under observation for at least five years and maintain a negative serology.

In the past year, I have been using a new preparation of arsenic, mapharsen, and am impressed with the results in a series of selected cases of early syphilis. It is well tolerated, does not cause the reactions so often seen with the older forms of arsenic, cleans up the skin lesions and brings about a reversal of the Wassermann with about the same speed as the old arsphenamine. What was of especial interest to me were the results attained in four cases of interstitial keratitis at the Springfield Hospital clinic. In each case the improvement in the eye condition was most gratifying in that the pain and discomfort were gone after the second injection and the congestion was much less. One case did develop a slight involvement of the other eye after eight injections. No one needs to tell me that four cases do not constitute a proved series any more than one swallow makes a summer, but when one looks back on the discouraging results in this condition with the other forms of arsenical therapy in the past, even four cases give me some hope to believe that this drug may be of decided value.

What does the adequate treatment of early syphilis promise to the patient? It is the adequate treatment of early syphilis that reduces or eliminates the later ravages of syphilis with which we are all familiar. In the survey made by the United States Public Health Service it was found that cases of neurosyphilis had, in most instances, been very inadequately treated with arsenic, and most of them had received little or no heavy metal. Their conclusion was that neurosyphilis was three times as common in those who had received "little" treatment as in those who had received "much". Early mucocutaneous relapse was seven times as common under like conditions. Late syphilis as relapse was entirely absent in the group which had received "much" treatment. In a later report, published in April, 1936, it is stated that it is apparent from the studies made by the service of a large series of cases, that the patient adequately and regularly treated for early syphilis will be almost exempt from cardiovascular involvement later. In respect to these conclusions it should be noted that what they call "much treatment" consists of twenty, or slightly over, injections of arsenic and forty to fifty injections of bismuth. I believe the thirty to forty arsenicals and sixty to one hundred bismuths paint a better picture in end-results.

Perhaps all pregnant syphilitic women do not come under the classification of early syphilis but the syphilitic baby most certainly does. It is an established fact that the luetic mother put under treatment by the end of the third month and treated throughout the pregnancy will, in most instances, produce a healthy child. All pregnant women should have a Wassermann early in each pregnancy and if found positive, or known to have syphilis, be put under treatment. Many doctors fear that their more affluent patients may be insulted if they suggest a Wassermann. It would be far kinder to insult them with a Wassermann early than a luetic child later. The poor are more fortunate as they go to a prenatal clinic where the Wassermann is routine.

SUMMARY

Syphilis is not a rare disease and no one is immune.

The dark field should be made use of much more frequently as a means to an early diagnosis.

Every case of gonorrhea, or chancroid, should be examined for the possibility of mixed infection with syphilis.

Early, intensive and continuous treatment renders the patient noninfectious and hence prevents the spread of syphilis.

Adequate treatment will probably reduce the incidence of neurosyphilis to ten per cent of its present prevalence.

Adequate treatment will probably almost eliminate cardiovascular and other late forms of syphilis.

Congenital syphilis is nearly an inexcusable disease.

The doctor has a most decided responsibility to his patients with early syphilis. Will he accept it?

DISCUSSION

CHAIRMAN TOWLE: This paper is now open for discussion.

DR. N. A. NELSON, Boston: It seems to me that Dr. Sullivan's paper has this particular value—that it calls the attention of this group of dermatologists and syphilologists to a situation with which Dr. Sullivan has been constantly impressed during his 18 or 20 years at the Springfield Clinic. You know as well as he that patients come to the attention of syphilologists and clinics whose infec-

tions with syphilis have been misdiagnosed, mistreated and mishandled generally by the physicians who had previously seen them.

It seems to me that a special committee could be appointed by this Section whose duty it would be to prepare material to be published in the name of the Section for the purpose of teaching physicians, in general, how to manage syphilis. I am of the opinion that such a group as this should be teaching obstetricians, for instance, that the treatment of syphilis in pregnancy is essential to the prevention of congenital syphilis; should be teaching pediatricians that there is such a condition as congenital syphilis; and should be teaching that the treatment of any form of syphilis is a part of the practice of medicine.

There are reported annually in Massachusetts more than 5000 cases of syphilis. Approximately a third of the cases reported are in the primary and secondary stages; that is, nearly 2000 early cases. There are approximately as many cases of congenital syphilis reported annually as of diphtheria, although syphilis is very poorly reported and diphtheria very well reported. The prevalence of infantile paralysis, which gets double headlines across the page whenever a case appears, is nothing as compared with the prevalence of congenital syphilis.

I bring to you the challenge of the American and Massachusetts Neisserian Medical Societies which are attempting to teach the physicians of the United States and of Massachusetts something about the management of gonorrhea. There is most certainly a similar problem to be solved in the control of syphilis, and if advice and information and assistance are to be made available to those physicians who know little about the disease or its management, it seems to me it ought to come from this group.

(Dr. Austin Cheever commented on Dr. Sullivan's paper and cited his experience with two cases.)

Dr. Joseph Muller: Dr. Sullivan's most admirable paper certainly was a challenge to us. We bear down in this State rather on tuberculosis, but we don't do anything about syphilis. Now I was educated and started my work in a country which did curb syphilis. Due to their poverty they couldn't do anything with tuberculosis. Their death rate is the same as it was in 1900, but at the same time they did see the challenge of syphilis, and they have made wonderful strides combating it. They brought the study of syphilis into their medical schools as a major subject. It was easy for all medical schools supported by the State. Where there is compulsory reporting of cases with the name of the doctor who treated each patient, treatment is enforced. So, the syphilis rates are coming down. Every one of us could bring up dozens of cases like Dr. Dennie did, and it is remarkable how often they are from the best families, as considered by the profession.

Dr. Lane: I commend Dr. Sullivan for urging very plainly this question of early syphiiis. I endorse all that he says in regard to early diagnosis and early treatment, and I think his discourse should have widespread distribution. He suggested leaving the matters of sex hygiene, and so forth, to the public authorities. I think that all doctors and dermatologists in particular should also participate in this field, not only to distribute information among other physicians, but also to the public as well. I think that is something for the whole medical profession to participate in. The matter of early diagnosis is, of course, absolutely essential, and the simplicity of dark field technic and the need for doing it universally, cannot be emphasized too often.

I also endorse what others have said in commentary about the Wassermann. I think that perhaps the too frequent Wassermann is a highly dangerous thing. The less frequent Wassermann is probably of advantage in numerous ways. I was very much interested this last week in a paper concerning something which I think many of us fail in, and that is the matter of epidemiological study of our cases. I think we should at least institute it, if we ourselves do not make an epidemiological study of our cases. That was emphasized very well in a recent paper in regard to the epidemiological study and a description of some of the cases by Dr. Dudley Smith of Virginia, by means of charts and work which he has done. It was surprising to find the contacts which he had been able to discover. Doctors do, however, see the original sources, but perhaps there are three or more contacts, and these contacts have several contacts apiece from which to trace the secondary sources. They go back perhaps through three or four generations of contacts. In one of his charts he showed fifty exposures which had been obtained from one patient, and one of his charts went back through one hundred different contacts which he was able to trace down and observe in the course of his study of an individual case.

It has been regrettable to many of us that at Harvard, they have cut down the number of lectures in dermatology and syphilis to five, expecting the student to be taught a knowledge of dermatology and syphilis in that length of time plus perhaps ten sections of the Clinic work. Of course, some syphilis is given in medicine, but no other teaching, so far as I know, covers the subject of adequate diagnosis of early cases. I hope that sometime we will be able to rectify this state of affairs.

Dr. G. A. Dix, Worcester: I cannot resist the temptation of saying a word about the matter that Dr. Lane brought up, and that is the social education of the early patient with syphilis. Now I cannot make myself feel that it is the business of either the Board of Health or the social worker to go into that. They may know some parts of it, but not all. When it comes to a case of telling patients about marriage, for instance, and about their other social and industrial contacts, we know more about that than the Board of Health and social workers do, and it is our duty to teach these people, what they are to expect from the disease and how to protect their associates. We talk a great deal, one to another, and in papers about the proper scientific treatment of syphilis. But I sometimes think we don't tell one another enough or teach our students enough about the natural history of the disease because really that is a very important part of treatment. The medical treatment of syphilis is not very difficult nor its special type so particularly important, but the social management of it is of decided importance.

Dr. Roy H. Peck, Springfield: It was with great pleasure that I listened this morning to my old friend and hated rival in Springfield, and perhaps I enjoyed his paper more because I certainly agree with him.

In the diagnosis of syphilis by inspection of the initial lesion or so-called chancre, we find it may take any form, and we don't expect always to see the clinical indurated sore of the textbooks. I have seen what appeared to be a simple balanitis show a dark field positive for syphilis. The only typical chancre is a lesion showing *Treponema pallida*.

Many times I think that we give too small doses of arsphenamine, and this results in a "fast" for arsenic. Too many Wassermann-fast cases are seen

with a history of thirty or forty neoarsphenamine injections of light dosage in conjunction with bismuth in some form.

Don't forget the old standby mercury in the treatment of syphilis, it still has its place in our armament and a strong one. It will many times comfort us in Wassermann-fast cases.

I have seen the maternal blood positive while the blood taken from the cord was negative. I can hardly understand that. Perhaps it is a fault of the laboratory.

I remember an instance that happened while endeavoring to ascertain the length of time arsenic was excreted by the kidneys after an injection of arsphenamine. Arsenic was reported in the urine for quite some time. Then the urine of a gonorrheal patient was substituted as control, and this urine was returned as containing arsenic. A checking over of the zinc used in the laboratory test proved the source of arsenic. It was found that the urine became negative for arsenic in five to seven days after the injection of arsphenamine. So why not make our intervals between doses from four to six days?

The treatment of syphilis takes time and I feel that progress should be checked by frequent blood tests and if the tests are negative tell the patient, it makes him feel better and if the explanation is made plain to him that this negative report is only showing good progress, but not a proof of cure, I hardly think many patients will discontinue treatment feeling the disease is eradicated.

THE CHAIRMAN: Dr. Sullivan will close.

DR. SULLIVAN, Springfield: Many times I have wished that Dr. Wassermann had been dropped in the Bay the day he was born or that he had never discovered this test because just as soon as you get a negative blood they say, "I don't need any more treatment," and you have to spend hours trying to sell them the reason for more treatment and that a negative blood has very little significance in these circumstances.

As regards the problem of sex hygiene, I assumed that everyone realized that while we practice medicine many of us are also associated with the societies that are interested in this other phase of the subject. On this matter of congenital syphilis I wish to tell one interesting case. Of course the Bible says that the sins of the fathers shall be visited upon the children even unto the third and fourth generations, and I wish to prove to you that this is not always true. About three years ago there came to our Clinic a young man with a typical chancre about the size of a walnut of six weeks' duration on his lower lip. I accused him of having been exposed to dissolute women but he assured me that he was married. I replied that while I knew that the marriage vows were supposed to act as a moral restraint I had never observed that they were a positive physical deterrent. He maintained that he had done nothing of the kind suggested so I told him that he would have to bring his wife in and he said that she and also a child were with him. After I had started him on his way to treatment I saw the wife and child. The wife was a very good-looking and very healthy-looking young woman of about twenty-three, but in her arms she held the most complete example of a luetic child you ever saw. The peculiar thing about this child was that when the child was thirteen months of age the lesions were the type that is seen in the first two to three months of life and they did not develop until the child was eleven months old. Here was a case where the father had acquired his syphilis from kissing his own child. It was the sins of someone being visited upon the father through the child.

Then I asked this young woman, or rather I didn't ask her, I told her. It is a mistake to ask them if they ever had it, they won't admit it. I said to her a number of years ago when you were only fifteen or sixteen you had intercourse with some man. She said this was true and then I asked her what became of him. She replied that one day he left that small town suddenly and had never been back. That fellow knew that he had acquired syphilis and knew that he had infected her and so he just disappeared. She never had any outward symptoms of syphilis but she did remember that for about a year she did not feel well and that her doctor gave her tonics for anemia. Six or seven years later she married. She had had her syphilis long enough so that she did not infect her husband but when she had a child it was necessarily syphilitic and that child infected its own father.

The point of all this is that if this young woman had a Wassermann when she became pregnant she would not have raised a syphilitic child and imposed the disease upon her husband. Some doctor made three cases of syphilis where there should only have been one.

THE CHAIRMAN: Before we adjourn for luncheon let me remind you of the round table discussion.

(The Section then adjourned.)

NEW HAMPSHIRE MEDICAL SOCIETY

THE PRESIDENT'S ADDRESS*

BY CLIFTON S. ABBOTT, M.D.†

IT is an established custom of this Society to listen to remarks from its President at this time on matters that he deems important for the good of the Society. The Society is a democratic body with functions both educational and economic. The function of its meetings have always been primarily for the discussion of the scientific phases of medicine. But of late years the economic stress of the times should necessitate some considerable time being given to the discussion of matters relating to social and political economics either in the meetings of the House of Delegates or in the open meetings of the Society.

There is no doubt but that there are many people in the low income groups too prosperous for relief, but who are unable to budget their affairs so that they can meet emergencies when they arise. They delay in seeking surgery, and take serious chances with disease that may endanger their future health to an extent that is beyond recovery. A serious illness can easily take a heavy toll from one's bank account, and if the bank account has been depleted by supplementary low wages and short time employment, as well as by living expenses, a severe illness will leave the family badly in debt. This condition confronts so many individuals and families that there is ample excuse for them to seek more economical medical service. Economical medical service will have to be good service, however, or it will become most expensive, and a menace to the welfare of the community itself.

As far as actual happenings having occurred, this has been a quiet year, but we have plenty of evidence that the present plan of practising medicine is being studied, evidence collected, and facts evaluated by lay organizations, with the altruistic claim of improving our medical service to the sick, which to them means insurance under federal control. It is claimed that since the economic depression, while the same high standards of medical practice exist, there are more people unable to pay for it, or more people that will require a long time to pay for it, so that the study of this phase of medical practice is an entirely proper thing, for it is universally admitted that there can be no prosperity of nation or family without good health.

The basic principle that must be borne in mind is to provide adequate and skillful medical care for all the people at a price that they can afford to pay, and at the same time to secure for the doctor an income that will enable him to keep himself professionally progressive and physically fit.

The medical profession should not leave the study of its activities and the furtherance of plans for improvement to lay bodies alone, but should, with open mind, study the situation themselves, for if it is true that a man thinks clearly only in the line in which he has been trained, the doctor should be able to plan the solution better than anyone else.

The doctor has a bad reputation as a business man, but he is improving. There are capable business men in the profession.

In applying this discussion to New Hampshire, the industrial sections of the State have suffered from poor business and consequent short time employment and low wages, resulting in many people with badly depleted bank accounts, and more on relief.

The American Foundation asks us if we think any radical change in the present system of the practice of medicine is necessary or desirable in New Hampshire. Here the greatest part of the work of caring for the sick is done by the general practitioner, and all of the surgery and the majority of the cases of severe illness are cared for in hospitals.

The people of New Hampshire are hospital-minded. More and more the hospital is being utilized. This is shown by the fact that New Hampshire has thirty-eight hospitals, well distributed over the State; twenty of them are approved or provisionally approved by the American College of Surgeons. The hospital offers facilities for diagnosis and treatment of disease that cannot be duplicated in the home, and is of mutual benefit to both doctor and patient.

We are living in a time when rapid changes occur. We have to keep alert and attuned to them or we find ourselves out of sympathy with conditions. It is said that prior to 1870 changes took place very slowly, and since then there has been an ever-increasing rapidity of change in customs and thought. Medicine is bound to change with other customs.

The family physician in the true meaning of the term is nearly extinct. It is unusual for a doctor to have a whole family that he can depend upon for patronage for any length of time, while some years ago it was not unusual for a physician to care for the family, their

*Read at the Annual Meeting of the New Hampshire Medical Society at Manchester, May 26, 1936.

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children and grandchildren, and from this experience to acquire facts that were valuable to him under certain conditions of disease. But under the modern conditions of easy, rapid transportation, telephones, hospitals and the vast increase in medical knowledge, the public does not pin its faith on any one man. The family physician's place has been taken by the general practitioner, who is, or should be, a diagnostician, and capable of guiding his patient in serious or unusual illnesses to various specialists, and capable of evaluating the various opinions rendered by them. There is a common saying that 80 per cent of sickness can be diagnosed and successfully treated by the general practitioner alone, but obviously this means the vast number of minor ailments that recover quickly, for the majority of severe illnesses are treated in the hospital, where the patient can have the advantage of group conferences, laboratory, x-ray, and so forth.

The hospital is the most remarkable institution that organized medicine has developed for treating the sick,—one might say that the hospital *is* medicine, actually it is an institution in which the patient is assured of the best treatment available; at the same time it affords the doctor an opportunity for case study, and conferences with his fellow staff members that result in educational advancement to himself.

Under the wise guidance of the American College of Surgeons the hospital has become an established factor in the community, which the average citizen accepts as a matter of course, much as he does his other civic privileges. The family physician of a few years ago did not care whether he had access to a hospital or not, while today people look to the more or less closely connected group surrounding the community hospital for their medical care. No one wants to practice surgery or medicine who does not have access to a hospital, and the nearer a doctor can limit his practice to hospital and office, the more fortunate he is. Incidentally the hospital enables the general practitioner to become a part specialist. This is an important thing, for every general practitioner should strive to know some branch of medicine better than others. He should excel in some one subject, for the field of medicine is so vast and so complicated, that no one can hope to excel in all branches.

But is obvious that the hospital and its advantages have added to the cost of sickness. This might not be so if the patient would be contented to accept his care on a necessity basis, to eliminate luxuries and consider essentials only. But we find that the "keeping up with the Joneses" attitude exists here even more than in other walks of life. Expensive rooms, too long a stay, private nurses, where a ward bed only is indicated, and the employment of costly and unnecessary methods of diagnosis.

The essentials in a hospital are about as good for the poor as the rich. I have never found any great difference in the mortality rate of the ward and the private room. The objection to the ward is the lack of personal privacy, noise, visitors, and talk from other patients. Improvement in hospital construction, according to C. L. DeMerritt, in the *Atlantic Monthly* for April, 1936, would be the construction of very small rooms, or two or three bed wards, that could be let at a reduced rate, and thus overcome the objections to the open ward as listed above.

Many patients leave the hospital with empty pocketbooks, and even in debt to the institution itself. Of necessity they either ignore the doctor's bill, which is usually very small in comparison with the hospital charge, or put off the payment of it to the distant future.

GROUP HOSPITALIZATION

One out of every fifteen requires hospital care every year. That involves one-half the cost of medical care for the entire family. Sickness is a thing that the family never provides for in its budget.

The greatest cost of sickness comes from cases involving hospitalization. It is obvious that hospitalization is a necessity in many cases. This being admitted, it would seem that the most practical way to reduce the cost of sickness is to reduce the cost of hospital bills.

The plan of Group Hospital Insurance was presented to you some two years ago by Dr. Metcalf, and was officially approved by the House of Delegates last year. Since then it has been studied and practical details elaborated by the Committee of Hospital Superintendents, Mr. James A. Hamilton, Chairman. The Committee thinks well of the plan and believes that it should be put into operation. This is no experiment. It is successfully operated in many places in this country. It has been found that the plan succeeds best in thickly settled communities, where there is a considerable cross-section of the population to enroll. So, in recommending the same for New Hampshire with its small population, I believe that group hospitalization, if adopted, must be inaugurated voluntarily by a few hospitals in different cities and towns as a purely local enterprise. If the scheme works out well, hospitals in other cities and towns will gradually be forced to fall into line, so that group hospitalization will eventually become more or less statewide. I believe that this plan is the most practical that has so far been offered to reduce the cost of sickness to the low income group. I would recommend that effort be made to put this plan into operation in the early future.

There are many other plans and experiments being conducted by medical societies in various parts of the country.

The treatment of patients by groups, so formed as to cover the various specialties, saves duplication and the overhead is estimated to be reduced about 20 per cent.

There is a plan in operation in Washington, D. C., that has the enthusiastic support of the medical society of that city, and is being adopted in some other large cities. It would not be practical, without considerable modification, in small cities and rural communities.

This plan co-ordinates the medical resources of the District of Columbia, doctors, hospitals and dentists, with the aid of the Community Chest for the purpose of making adequate medical care available to all that need it at a price that they can afford to pay. This recognizes three major situations—1. The care of indigents. 2. Cost of hospitalization and nursing to nonindigents. 3. Payment of medical services by small wage earners.

1. The sponsors believe that the care of the indigent is a local obligation, state or county, not federal.

2. The cost of hospitalization and nursing is met by a group hospitalization plan.

3. Payment by small wage earners is arranged through a bureau called "The Medical and Dental Service Bureau." Here the budgeting of the doctors' and dentists' fees is done. Arrangements are made by the Bureau in accordance with the finances of the patient as mutually agreeable to both patient and doctor.

We cannot deny that there is a great interest in socialized medicine in this country. Sickness insurance has been in force in leading European countries for some years. The coverage in England is limited and restricted to the lower scale of wage earners, while that in Germany is a very complete coverage. I understand that the German plan is the one in favor with those that are back of the movement in this country. There is a well-founded objection on the part of American doctors toward compulsory health insurance. This is based on the knowledge that where this has been tried it has not worked out to the advantage of the doctor, or resulted in a better grade of service to the sick.

Medicine, under state control, has many features that make the thoughtful man wish to avoid it.

Looking at the situation from a different angle, as a matter of the prevention of disease, the Committee on Legislative Activities of the American Medical Association suggests:

"The social aspect of sickness connotes the broader problem not entirely medical. Adequate income provides for normal living and working conditions, and a reserve for emergencies.

"Insufficient income and unfavorable employment conditions reduce the family to a poor living level, with insufficient food, inadequate clothing, unhealthful housing, bad psychogenic states. Subnormal health follows; less effective work is a consequence.

"Sickness especially disabling, as tuberculosis, heart disease, arthritis, is much more frequent as a result of the above conditions.

"Absence of a reserve necessitates frequent expensive care in public institutions. Disability creates partial or complete dependency.

"Medical care cannot elevate the individual to normal health and effective work when unfavorable living conditions make this impossible.

"Sufficient income for normal living to reduce sickness would be more effective than a few weeks of medical service after chronic disease and permanent disability are established."

If our well-wishers, the Government, sociologists and philanthropists could stimulate business to an activity where there was a real demand for labor, with high wages, the purchasing power of the masses would be restored, and the problems incident to poverty would cease to be troublesome. If it is necessary to change or modify our present plan of practicing medicine so as to distribute the cost of medical care from the individual to the group, the plan should be in charge of the medical profession. If economic conditions do not improve, it is apparent that some change will have to be made. The matter is of enough importance to merit your thoughtful consideration.

THE IRRITABLE COLON: DIAGNOSIS AND TREATMENT BY THE GENERAL PRACTITIONER*

BY J. DUNBAR SHIELDS, M.D.†

THE purpose of this discussion is to emphasize the importance and prevalence of the condition, "Irritable Colon," to call the general practitioner's attention to the necessity of recognizing and treating the condition in its early stages, to make some suggestion as a means of diagnosing the condition without the help of elaborate laboratory apparatus, and to offer a method of therapy applicable to ambulatory office practice.

We are considering a very common condition, which, although often unrecognized and therefore often mismanaged, is easily diagnosed if the physician will only remember to keep it in

*Read at the Annual Meeting of the New Hampshire Medical Society at Manchester, May 26, 1936.

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mind as a possibility. A great deal has been written on this subject during the past months, but it has been too often presented from the standpoint of hospital diagnosis and therapy. The contention of this review is that if recognized and treated early, the irritable colon can and should be handled adequately by the general practitioner in his office.

Colon difficulties are common, and of all the colon ills, the one discussed in this paper is the most common. Approximately four per cent of the patients treated in my office during the past two years have had irritable colons. If you stop to consider the various complaints, including everything from a common cold to advanced carcinoma, which bring the patient to the office of a general practitioner, you will probably agree that four is a percentage high enough to make the condition warrant consideration. Its prevalence has been recognized in reports in the literature. Jordan and Kiefer[1] find that thirty per cent of three thousand admissions to the Gastro-Intestinal Service of the Lahey Clinic were proved cases of unstable colon. A large percentage of patients who come to the physician's office with vague abdominal symptoms associated with a neurosis, who are given some type of pill and sent away, could then be greatly relieved if properly treated for irritable colon.

As stated above, most of the attention which has been called to the subject has been along the lines of hospital treatment and therapy. The case which reaches the hospital or large clinic is, as in all other conditions, usually more advanced and of longer standing. We are emphasizing more and more the importance of early diagnosis and preventive therapy in all pathologic processes. Why should it not be of just as much importance in this condition, as it is one which is so common and one which is apt to progress if not treated intelligently? Because of the etiologic factors associated with the disease, its early diagnosis and treatment seem to be most important. It appears to be generally conceded that there are two very important factors in the production of this disorder, namely, the neurotic background and the cathartic habit. Probably the more important is the neurotic background.

Eggleston[2] concludes that the unstable nervous system is the most prominent etiologic factor. Laus[3] describes a so-called irritability threshold determined by the individual's make-up and exaggerated by irritants. Jordan[4] also finds a very definite relation between unstable colons and a neurosis. There is a tendency to a nervous imbalance in the individual which is exaggerated either by psychic or physical irritants.

The most important physical irritant is the cathartic. The cathartic habit is the result largely of pernicious advertising which, as Hurst[5] aptly expresses it, "accuses the colon of ills it never commits", and the result of mass suggestion from constant reading about the disastrous effects of intestinal intoxication is that most of the lay public and many of the medical profession join in the slander. The already unhappy colon is whipped into an enraged and stubborn state. If the case is allowed to progress untreated, the digestive and bowel distress may cause a neurosis and constipation which, following the taking of cathartics, create vicious circles which tend to make the case much more intractable.

As to the method of diagnosis the most important conditions are the history and evaluation of the patient's general make-up. Physical examination is of some help, and laboratory examination is of great help if it can be employed. However, as this is a condition so universal and as many practitioners have not the advantage of x-ray equipment, I would like to call attention to the fact that, although the x-ray is an invaluable aid in diagnosis, it is not essential. Almost all articles in the literature make the statement that every case should be thoroughly x-rayed. I feel that this is true certainly of hospital practice, because, in most of these cases, symptoms are so advanced that an x-ray examination is necessary in order to rule out associated conditions, particularly the malignancies. However, if a roentgenographic examination cannot be made, the physician should recognize and treat the condition intelligently rather than give cathartics and thereby aggravate the symptoms.

As we know, the colon is enervated by the two parts of the autonomic nervous system. The parasympathetic, originating chiefly from the cranial nerves, has a pressor action upon the intestinal tract; and the sympathetic, originating from the spinal nerve roots, has a depressor effect. These two systems are very delicately balanced, and this balance is quite easily upset in the individual of unstable nervous tendencies. The disturbance of this balance produces the syndrome exemplified by the patient of unstable nervous make-up who gives a history of constipation or diarrhea, vague abdominal discomfort or pain associated with gaseous distress. In more extreme cases, nausea and vomiting, and often anorexia and loss of weight occur. The symptoms which brand the patient as being one of those individuals of unstable nervous balance are too legion to be enumerated; among them, however, may be mentioned vertigo, depression, headache, fatigability, insomnia, irritability, and palpitation. Another point which has, I think, not been stressed enough is the fact that a large percentage of these individuals suffer from attacks of migraine. This headache is quite apt to occur in the early

morning; in fact the patient usually awakens with a headache which is often associated with nausea and vomiting. Kiefer[6] has called attention to this, saying that migraine is frequently associated with constipation; and although the migraine patient may or may not correspond to one with the typical type of spastic colon, the association is too frequent to be merely coincidental.

Physical examination sometimes reveals tenderness over parts of or the entire colon. Occasionally a rope-like sigmoid may be palpated. Other than these findings, the physical examination is valuable chiefly in ruling out other disorders.

We will not go into the x-ray findings. Suffice it to say that the barium meal and barium enema give interesting and valuable diagnostic aids.

As to treatment, I would like to emphasize first and foremost that as the two most definitely established etiologic factors of this condition are nervousness and bowel irritants, the treatment should primarily attack these two causative factors.

Dunham[7] states in speaking of mucous colitis, which is so often associated with this condition, that re-education for the purpose of drawing the patient's attention away from the bodily functions is the *sine qua non*. Unless the patient can be made to understand that he has no serious organic disorder and that his disorder is curable largely by his own effort, your psychotherapy will be unavailing.

I usually, in the beginning of the treatment of these cases, plan to give at least one-half to one hour's "pep talk", during which time I first emphasize to the patient that there is no indication or evidence of severe organic disease. I consider this first step to be of utmost importance. Next I try to give him some idea of just what his condition is, even explaining in most cases by diagram the nervous control of the intestinal tract, and then I emphasize the importance of not distributing this delicate nervous balance. This explanation usually does two things: it obtains the patient's confidence by showing him that you do not consider him a faker or malingerer, and, secondly, it proves to him the inadvisability of the prolonged use of cathartics. I next emphasize very completely to the patient that his habit of taking laxatives, which may run back over a period as long as fifteen years, must be stopped completely and abruptly. To do this it is necessary, as stated above, to show the patient why, and it is also necessary to convince him thoroughly that bowel movements are possible without cathartic stimulation. This is usually much easier than it would appear.

Psychotherapy along general lines is invaluable. Teaching these people how to live and how to control the emotional imbalance and the removal of all possible emotional irritants is important. It is sometimes possible practically to cure cases with this alone.

Although these psychic problems are of utmost importance, habit formation, diet, and some medication are invaluable. I have adopted the plan of giving the patient numerated written instructions to be followed implicitly. For the sake of brevity I will give these now, and they will be self-explanatory. They are as follows:

1. Take no enemas or laxatives.
2. Drink two glasses of warm water at bedtime and two on arising, and drink as much water both with and between meals as possible.
3. Establish a definite bowel habit by going to the toilet immediately after breakfast every morning and remaining there for at least twenty minutes regardless of whether the bowels move.
4. Follow the diet list carefully and report in one week for a change in diet.
5. Take fifteen drops of tincture of belladonna in one-quarter of a glass of water, increasing one drop per dose each day until symptoms of dryness of the mouth or dilatation of the pupils occur. If these occur, report back for change in dosage.
6. Take two teaspoonfuls of parapsyllium (white medicine) every morning and every night until a change of dosage is ordered.
7. Arrange your activities so that it will be possible to get at least forty-five minutes complete relaxation in the middle of the day. By this I mean lying flat and as relaxed as possible on a bed or couch.
8. Purchase one pint of cotton-seed oil, and if bowels do not move during the day, instill one-half a glassful of warm oil into the rectum before retiring and allow it to remain until morning.

After giving the above instructions it is a very good idea to discuss them individually with the patient; for instance, it is quite necessary to explain to them that it is possible for them to get along without the use of enemas and laxatives. Unless this is very forcibly impressed upon their minds they will continue in the cathartic habit.

In the second paragraph of these instructions emphasis is laid upon the drinking of water. It will be found that a great many of these patients drink relatively very small quantities of water, and the addition of large quantities of water to their diet will in itself contribute toward making the stools much less constipating.

There is a certain per cent of these individuals whose occupation is such that they have

never formed a regular bowel habit routine. They have for a long time neglected the reflex stimulation of a full rectum, thus lowering the threshold to such a degree that they do not respond to this normal stimulus. The formation of a regular bowel habit, as explained in the third instruction, is of great value to these people.

The diet list is quite an important feature of the treatment. It is made up of nonirritating, low residue foods with the idea of producing as little irritability of the bowels as possible. I begin with a strict bland low residue diet with vegetables puréed.

The use of belladonna seems to be quite rational in that its action in paralyzing the parasympathetic nerve endings is of great value in correcting the imbalance which exists between the parasympathetic and the sympathetic divisions of the autonomic nervous system. I go on the theory that different patients exhibit different tolerances to the drug and therefore start on a small dose, increasing it until actual physiologic effect is obtained. There is another reason for giving belladonna, and that is that when given in large enough dosage, it also has a tendency to increase thirst, and therefore facilitates the intake of water.

Some authorities will disagree with me in the use of the mineral oil psyllium seed mixture, saying that mineral oil has a tendency to be a bowel irritant. I have not found this to be the case when used in the above dosages. In office practice where it is not possible to check up on the patients as to the taking of enemas or laxatives, it is important that we get immediate results. If the patient finds that he has no bowel movements after a period of three or four days, he will most probably turn to some type of laxative. By giving parapsyllium, this danger is partially removed. It is my practice to reduce this dosage within a period of four days, and continue gradually to reduce the dosage so that within a period of ten days to two weeks it becomes unnecessary for him to take this medication. It is found that, after suddenly reducing the bulk of the diet, as is done when the patient is put on a low residue diet, there is not sufficient bulk in the intestinal tract to produce a normal bowel movement. The parapsyllium is given with the idea of making up this bulk in a bland, nonirritating mixture. As the dosage of this is reduced, the bulk is gradually made up by adding slightly more residue to the diet in the form of lettuce, celery, and stewed fruits. As the case progresses, the diet is further changed by the addition of vegetables of higher residue or by the discontinuation of the necessity of using purées.

The seventh instruction as to relaxation is very necessary. In hospital practice this is taken care of by bed rest. In treating the ambulatory case, the actual rest in the middle of the day seems to be of great value in reducing the accompanying nervous tension.

In some cases it will be found that the patient does not immediately respond to therapy and that the bowel movements are unsatisfactory during the first week or two weeks of treatment. The use of the cotton-seed oil rectal instillation often facilitates a normal bowel movement without producing untoward irritative effects.

Of course there will be many cases met with that offer individual problems and the care of which necessitates individual changes in the above therapy, but, as a general rule, the above therapeutic plan will fit every case with minor changes. This plan of therapy has been of great help to me and has almost unfailingly produced excellent results. No group of patients has been more appreciative than have these colon cases.

Summary: 1. The condition, irritable colon, is a very common one in office practice. 2. Diagnostic suggestions applicable to general office practice without elaborate laboratory apparatus are presented. 3. A method of therapy which I have found to be of great value is discussed in detail.

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DISCUSSION

PRESIDENT ABBOTT: The discussion of this paper will be opened by Dr. Clarence O. Coburn of Manchester.

DR. CLARENCE O. COBURN: I think that Dr. Shields' paper is very opportune. In fact, my experience during the past four or five years shows that this condition is becoming more prevalent than I had noticed before. Perhaps I was not so keen on making the diagnosis previous to that time, but it seems to me that it is mostly due to the stress, strain, worry, hurry and the methods of modern life caused partly by the depression.

I think another element that enters into the situation is fear. People nowadays have the phobia because of radio and newspaper advertising.

Another thing that produces fear and worry in these cases is the idea many people have, gained from literature and faddists, that they should have five or six movements a day, and that if they don't they will get intestinal toxemia. I think that bugaboo has been played to the limit. My experience has been that those who have one normal movement a day are much more healthy than those who have two or three.

As Dr. Shields has stated, it may be any condition in the gastrointestinal tract, with nervous symptoms and imbalance. I have often come in contact with the fact that many times people lay the beginning of their troubles to intestinal grippe; they think that is the cause of the difficulty.

The physical examination, as Dr. Shields has told you, does not generally show very much. The thing that I have found most constant is a tender cecum, or tenderness along the colon. I generally do a rectal examination, because I have found many of the cases of rectal irritation that way, with perhaps a fissure. There may be an element there, whether it is the cause or the result I am not sure, but I think it is the result of taking cathartics and of constant irritation around the anus.

In making a diagnosis of irritable colon, I think it is really a process of elimination. It seems to me to be an elimination of all other conditions which may happen in the intestinal tract. These conditions have often been misinterpreted. I have treated a supposed case of duodenal ulcer, without x-ray finding, which proved later to be an irritable colon. I think that is quite apt to be the case. They simulate some other condition.

In the treatment, I agree entirely with the doctor's methods. Regulation in life is the prime essential, that is the method of living. In these days of hurry and scurry to get a livelihood, many do not take the time to have a regular bowel movement. Many are so worried and depressed at the time of meals that they do not take the time to eat properly. Further I believe that rest after a meal is very essential, and also the elimination of all aggravating factors, such as tea, coffee and tobacco. Focal infections may also be undermining the patient.

As to the medication, I do not think it makes much difference what kind of emulsion is used; anything that is a soft and nonirritating lubricant seems to me to be sufficient.

In regard to the use of belladonna, I think that it is very valuable. I often supplement this with small doses of phenobarbital. These prescriptions cannot be refilled, and I so mark them for the attention of the druggist. The druggist will not refill these prescriptions unless the patient has been back to the physician to be looked over again.

There is just one other thing I wish to say that may not appeal to all of us. I have seen many cases operated upon for many different intestinal conditions. Appendicitis is the most common. After the rest and the diet which the patient has in the hospital following such an operation, he generally improves, but in several months, he is right back again in the same condition. I think that we should be very careful about that, and have a diagnosis established before operation.

PRESIDENT ABBOTT: This paper will be further discussed by Dr. Fred E. Clow of Wolfeboro.

DR. F. E. CLOW: Dr. Shields is to be congratulated on the attitude he takes toward the victims of a disease with a new name, who have haunted the consulting rooms of doctors for years. Axel Munthe describes with gusto his management (for his own pocketbook) of the rich women of Paris who had colitis. Each generation has furnished its own name for the same old disease. The approach to its treatment by younger men is evidence of the fact that they recognize its etiology and its dependence on the nervous system to a great extent.

Constipation, well-nigh universal among women, with pernicious cathartic drug habits grafted on a maladjusted personality, is sufficient to produce a train of most annoying and disabling symptoms. During the last few years it is obvious that high roughage diet has increased the severity and it would seem the frequency of these difficulties.

Nothing can approach transduodenal lavage with hypertonic solutions for relief of the migraine that so often goes with an irritable colon. The thorough cleansing of the entire intestinal tract is the most effective method of starting right. Fluoroscopic examinations of the colon are important. The importance of this has been stressed in connection with a study of the patient's face. Hospital treatment, unless one is ready for a long campaign, is dangerous. These are the people who easily become habituated to a nursing routine from which it is difficult to dislodge them, unless one is an expert in psychotherapy.

Occurring as it does always in brain workers, school teachers, lawyers, and women with too much time and too few children—those, to quote Trice, "individuals of ambition with keen desires, and among those who grieve and fret," the etiology must never be forgotten. The origin of the irritability must be sought not in the intestinal contents, not in the bacterial growth, but in the mind and brain of the patient.

PRESIDENT ABBOTT: The paper is now open for general discussion.

DR. LOUIS C. AGER: We have, at present, in the hospital at Rutland, a general medical service which has been recently established. All those patients coming in on that service go through my hands.

I noticed that the last speaker seemed to confine his remarks to women and to brain workers. We don't get brain workers in the Veterans' Hospital nowadays, to any great extent. We are naturally getting the down-and-out man, who has lost his job, and a large percentage of permanent derelicts. The high percentage of gastrointestinal lesions which we get, and which are so largely, as has already been said, purely a neurotic condition, is astonishing.

Of course, we have every facility there for x-ray work.

No man ever has chronic pain and tenderness in his stomach without a study by barium, if there is the slightest occasion for it.

I have lost my faith, to a considerable extent, in gastrointestinal x-rays. We almost invariably find a lesion of some sort. We have had particularly strange results on the question of duodenal ulcer. Apparently deformity or absence of the cap is the rule rather than the exception. It is the same way in the colon. We always get, with these patients, a rapid emptying of the colon.

The condition, we accede, is partly due to malnutrition, to improper or irregular food, together with emotional stress. But are there actual pathologic changes in all or may mere functional changes give the same effect?

These patients are all men, from thirty-five to forty-five years of age, in most instances. They are not brain workers. But mental strain will do most anything to anybody.

The reader of the paper did not distinguish, while I was here, between a mucomembranous colitis and an irritable colon. We don't see this condition in these men, but we do see many instances of spasticity of various sections of the gastrointestinal tract.

I should like to ask the reader of the paper if there is any real reason for shifting over from psyllium seed to agar, whether there is any particular difference, or just because the psychologic effect is good.

I have never seen the logic of the treatment of putting agar into the mineral oil. The agar is used to create a soft mass which will irritate, but some-

what dilate an irritable intestine which is often spastic. It seems to me the logical way is to get that dry and give the mineral oil to separate it.

One other point to be borne in mind is that you cannot tell all of these patients to drink all the water they can drink; they have a mental bias against this. Perhaps you don't meet that trouble outside, but I have seen it repeatedly in the hospital.

PRESIDENT ABBOTT: Is there further discussion on this paper?

DR. STEVENS of Manchester: I would like to say a few words on Dr. Shields' excellent article, from a psychiatric point of view. In a general psychiatric practice, we find that almost every neurotic and near-psychotic patient has some sort of an intestinal problem. The situation seems to tie up with the inability to make a success at the higher reality level.

If we consider the normal development of the aggressive impulse in each individual, we find that in early childhood, it flows through, in infancy, the mouth level, and goes on, to the bowel level; so that the accomplishment of the infant in biting and taking in food at a later date is the accomplishment in the nursery of evacuation. The child comes to learn that society puts a certain value on excretion, and the mother is usually very well pleased if the toilet requirements are met.

Later in life, of course, the aggressive impulse flows over into expressing itself in marriage, the birth of children, and, in the man, in the support of his family and the accomplishment of success.

When, for any reason, the individual fails to accomplish success at the reality level, perhaps due to the general depression or due to certain inherent difficulties in his own make-up, we frequently find that there is a going back to the bowel level, for the purposes of accomplishment. It is as though the individual retreats from a reality level and fixates on the bowel level, and, at that level, tries to solve all his difficulties.

The irritable colon seems to stress, more than anything else, an inherent constipation tendency, which has, unconsciously, a very strong self-preservative value. Now, that may sound rather silly, but the average neurotic, under psychotherapy, does place a certain value from the supportive sense on retention and you find, growing out of that same tendency, the habit of miserliness; also the habit of playing the game of life pretty closely. These people are usually very formal; they are not generally aggressive, and not the sort of people who take a chance.

The constant worry over cathartics, of course, relates to the social conscience which is against the retention. Most of these cases can be traced back to an overemphasis on the toilet function in the nursery, with a mother who was very vigorous, indeed, in her training methods, or else one who was extremely lax.

PRESIDENT ABBOTT: Because we are running a little behind our schedule, I am going to call upon Dr. Shields to close the discussion.

DR. SHIELDS: This has been a most valuable and interesting discussion of my paper, and I appreciate what has been said very much. It is a subject which is so broad and which takes in so many details that of course it cannot be discussed completely in the length of time allotted here.

There were some points brought out which were of very great interest to me. For instance, Dr. Coburn's observation that so many of these people have been operated upon has always been of great interest to me because of the fact that we find so many of them coming in with irritable colons who have had a whole series of operative procedures, with a return of their symptoms after discharge from the hospital, and, not only a return of symptoms, but usually an exaggeration of symptoms after each successive operation. That is one of the worst things in the world that we can do for them, to increase the psychic and emotional trauma by any kind of operative procedure. That is why the condition should be emphasized more completely and why the medical profession should know more about it.

Dr. Coburn also emphasized the fact that you have to treat the patient as a whole; that is, to take in all of the different reasons why the individual had these difficulties.

Dr. Clow emphasized the fact that a high roughage diet and the propaganda put out by the producers of foods have had so much to do with the production of this disorder, as well as the propaganda put out by the manufacturers of the different types of candy laxatives, and that they have all contributed toward a further irritation of the already irritable colon.

As to the question of why an individual who is not a brain worker has this condition, we do see it, probably more frequently in women, and we do see it more frequently in the brain worker, but I think probably the reason Dr. Ager sees so much of it is that he is dealing with people who do not have jobs, and who have nothing to do but think of themselves. That is the reason why he finds the condition so prevalent among the men that he sees; he has a type of man under his care whom we could expect to develop some condition of this sort.

The question of the choice of medication to give in the way of increasing the bulk of the bowel movements is purely a matter of personal choice. I think anything, agar just as well as psyllium seed, or any type of mixture used, is perfectly all right, as long as there is no added laxative. A great many of those preparations have added to them cascara, phenolphthalein, or something of that sort; these should not be used. It is purely a matter of personal choice as to which type of proprietary preparations are used to increase the bowel bulk. The ideal situation, of course, is not to use any type of medication and to get your patient, as quickly as possible, back to normal bowel function.

With the addition of roughage in the form of food, such as cooked fruits, cereals, lettuce or something of that sort, the condition may be brought more nearly to normal.

I am particularly glad that Dr. Stevens discussed this paper because the neurotic side of these individuals is, after all, most important. A great many times, I feel that I would give anything to be able to put these different individuals under the care of a competent psychiatrist. Unfortunately, we can't place them all under the care of the psychiatrist, and we have to do as much as we can for them along that line. I am particularly glad that he did discuss this phase of the problem and that he gave us some idea of the way in which their difficulties react upon their intestinal tracts.

RECENT DEATHS

JOHNSTON—CHARLES E. JOHNSTON, M.D., a resident of Portsmouth for two score years, died at his home there on June 29, 1936, after a long period of failing health. He was seventy-three years old.

A graduate of the Dartmouth Medical School, Dr. Johnston practiced for several years in Norway and

Brunswick, Maine, before moving to Kittery, forty-three years ago. He established residence in Portsmouth in 1895.

During the World War he served at Chickamauga Park, Georgia, as a Captain in the Medical Corps. He was a Mason, an Elk and a member of the Portsmouth and New Hampshire Medical Societies.

Dr. Johnston is survived by his widow, Mrs. Mary Noonan Johnston, a brother and three sisters.

STOKES — Dudley L. Stokes, M.D., one of the oldest practicing physicians in Rochester, died at his home there on June 25, 1936, of a heart attack.

Dr. Stokes was born in Freedom, N. H., in August, 1866, the son of Stephen and Esther (Mills) Stokes. He attended the public schools there and later graduated from the New Hampton school. He then attended the Dartmouth Medical School, from which he was graduated in 1888.

Upon graduation from the medical school, Dr. Stokes opened an office in Goffstown, N. H. He remained there for a little more than a year, during which time he married Miss Sarah Tyler, of Freedom. In 1891, he moved to Rochester and practiced there until the time of his death.

Dr. Stokes was a member of the Strafford County, the New Hampshire and American Medical Associations, the Dover Medical Society and the New Hampshire Surgical Club. He was also a 32nd degree Mason and a member of the Eastern Star.

Dr. Stokes is survived by his wife, Mrs. Sarah Stokes, and three children, Elizabeth, Dr. Leroy T., and Dr. Samuel H. Stokes, a dentist.

DOWNING — Arthur T. Downing, M.D., was born on October 22, 1877, at Hanover, N. H., the son of Lucien B. and Martha (Taylor) Downing. He was educated in the public schools of Hanover and at Kimball Union Academy in Meriden. He continued his education with an academic course at Dartmouth, graduating with the class of 1900. He then entered the Dartmouth Medical School. For a year he served as an interne in the Mary Hitchcock Hospital in Hanover and then moved to Barrington, where he practiced for two years. From there, he moved to Littleton, where he enjoyed a large practice up to shortly before his death on June 25, 1936.

In 1903, Dr. Downing took as his bride Miss Mabel Moore, of Plymouth, Vermont, and to them were born two sons, Everett and Allan.

On October 28, 1921, he was made a Fellow of the American College of Surgeons in recognition of the work he was doing at the Littleton Hospital.

Dr. Downing was a member of the New Hampshire Medical Society. Fraternally, he was a member of Burns Lodge, Free and Accepted Masons, of Franklin Chapter, Knights Templars and of the Ancient Order of the Nobles of the Mystic Shrine and the Consistory. He was also president of the Littleton Hardware Company, a director of the Littleton Savings Bank and president of the Building and Loan Association.

He is survived by his widow and two sons.

WATSON—Maurice Watson, M.D., aged sixty-two, a prominent Manchester physician, died at his summer home in Gilmanton on June 22, 1936.

Dr. Watson received his A.B. degree from Dartmouth College in 1897 and his M.D. from the Dartmouth Medical School in 1901. He was registered to practice in the State of New Hampshire the same year.

Dr. Watson held membership in the Manchester Medical Association and was a former member of the New Hampshire State Society. He was a Mason and a Shriner. A staunch Democrat, he was active in politics many years ago and at one time represented Ward 6 on the aldermanic board.

Survivors include his widow, Mrs. Martha (Parsons) Watson, and two sons, Henry P. and William H. Watson, all of Manchester.

LITTLE — Charles S. Little, M.D., for the last twenty-five years Superintendent of Letchworth Village, a state hospital for the feeble-minded, four miles from Haverstraw, N. Y., died at his home there on June 6, 1936.

Dr. Little was born on February 12, 1869, at Webster, N. H. He was graduated from Dartmouth College in 1891. After his graduation he was civil engineer for two years, then he returned to Dartmouth to receive a medical degree in 1896. In 1933 he received the degree of Doctor of Science from his Alma Mater.

Dr. Little went to Letchworth Village from Laconia, N. H., where he had been Superintendent of the State School for Feeble-Minded for several years. Previously he had been at the Tewksbury (Mass.) General Hospital and the Taunton (Mass.) State Hospital and the McLean Hospital near Boston.

Dr. Little was married twice. His first wife was Miss Tertia Wilton, of Hamilton, Ont., who died in 1913. In 1919, he married Miss Daphne Perkins, of Moores Corners, Mass., who survives him. He also leaves a daughter, Miss Barbara Wilton Little, and a son, Dr. Sherman Little.

Dr. Little was a member of the New Hampshire Medical Society, and the Belknap County Medical Society.

NORTON — Daniel C. Norton, M.D., died at his home in Manchester on July 4, 1936, after a lingering illness. He was in his fifty-fifth year.

A native of New Britain, Conn., Dr. Norton was graduated from Dartmouth College in 1904 and from the Dartmouth Medical School in 1907. A year of internship at the Boston City Hospital was followed by a year of study and clinical work at the Eye and Ear Infirmary in Boston.

In 1909, Dr. Norton established his residence in Manchester, where he remained until his death, building up one of the largest practices in the State and establishing a widespread reputation in his chosen field.

He was a member of the Manchester Medical Association, New Hampshire and New England Medical Societies, the New Hampshire Surgical Club and

the New England Oto-Laryngological Society and of the staffs of the Elliot and Balch Hospitals.

In 1909, Dr. Norton was married to Miss Susie G. Dowd, of Athol, Mass., who survives him, as do a son, Russell, and two daughters, Elizabeth and Natalie.

BAILEY — GEORGE S. BAILEY, M.D., was born in Wilton, N. H., on April 20, 1868, the son of Marcus and Helen Melita (Thompson) Bailey. He attended Hancock Academy and was graduated from the College of Physicians and Surgeons of Boston in 1899. He began his medical profession in Falmouth, Mass., and, thirty years ago, moved to Hillsborough, N. H., where he remained until the time of his death, on June 20, 1936.

Dr. Bailey was a member of the New Hampshire Medical Society and the American Medical Association.

He is survived by his widow, Mrs. Anna M. Bailey; a son, Morton S. Bailey, of Rome, N. Y.; twin grandchildren, and three sisters.

DO YOU KNOW ABOUT THE VOLTA BUREAU?

"We consulted several specialists, and all of them confirmed our fears, but none offered any solution of our problem." Thus the mother of a small deaf child wrote to the Volta Bureau. The sentence might be quoted verbatim from many letters written by parents of deaf or hard of hearing children, or by hard of hearing adults.

The knowledge that deafness is present and that it is incurable comes with the force of a major calamity. It is so crushing in its effect that something positive in the way of help must be offered immediately, if the individual is not to spend desperate years in a bewildered effort to adjust himself. The parents of a deaf child must be told that the child can be taught to speak and can be successfully educated, and that this education may be begun at home immediately, even if the child is not more than two years old. The parents of a child whose hearing is only slightly impaired must be given advice as to his adjustment. The hard of hearing adult must be told about lip reading, about hearing aids, about social efforts in his behalf.

The Volta Bureau was established for the purpose of furnishing all this information to those who ask for it. Its services are free. Alexander Graham Bell, the son of a hard of hearing mother, the husband of a deaf wife, the lifelong friend of everyone handicapped by deafness, used the money received as a prize for inventing the telephone to found the Volta Bureau so that anyone confronting the problems of deafness might be assured of help. Advice is given as to schools and preschool training, lip reading instruction, hearing aids, social contacts, psychological difficulties. While the Volta Bureau is not equipped to do employment service, it gives information in regard to the fields of activity that are open to the deaf and the hard of hearing.

The *Volta Review*, a magazine for parents and teachers of the deaf and for the hard of hearing, is on the reading table of many physicians. Pamphlets dealing with all phases of deafness except medical problems are available to all who ask for them. Lists of such pamphlets and sample copies of the magazine will be sent free of charge. The Volta Bureau is located at 1537 35th Street, N. W., Washington, D. C.

MAGGOT STUDY YIELDS NEW FACTS ON UREA

Digging deeper into the recent mystery of how blowfly maggots stimulate healing in stubborn wounds, a fact observed by surgeons during the World War, Dr. William Robinson of the U. S. Department of Agriculture now announces the possibility that urea, a well-known and widely distributed chemical, may be responsible along with allantoin for this remarkable healing produced by maggots.

Dr. Robinson has been investigating this subject in the Division of Insects Affecting Man and Animals, Bureau of Entomology and Plant Quarantine. He announced last year the discovery of allantoin in maggot excretions. He now finds that urea is present also. Preliminary tests indicate that the pure synthetic chemical by itself induces the same healing as maggots or allantoin. These preliminary observations, of course, must be supplemented by additional clinical tests by competent physicians—and this is outside the scope of the Department's investigations.

In an article appearing in the August number of the *American Journal of Surgery*,* Dr. Robinson cites case histories provided by physicians, surgeons and dentists, who have used urea solution in the treatment of osteomyelitis, gangrene, old ulcers, stubborn wounds, infected burns and nonhealing gums and tooth sockets. The reports are encouraging. If borne out by subsequent clinical tests, Dr. Robinson's discovery will be of great importance to the medical profession.—*Bulletin*, U. S. Dept. of Agriculture.

*Robinson, William: Use of urea to stimulate healing in chronic purulent wounds. Am. J. Surg. 33:192 (Aug.) 1936.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 22341

PRESENTATION OF CASE

First Admission. A nineteen year old native factory girl was admitted complaining of epistaxis.

Seven years before entry the patient had a sudden attack of right-sided and lower mid-abdominal pain for which an appendectomy was performed. The appendix, however, was normal and she was treated in the hospital for nine weeks for what was said to be "pus in the urine". Cystoscopy was performed and pyelograms made. She was discharged cured and remained well for about two years. For three succeeding years she had severe sore throat each winter. These attacks lasted about two weeks. Two years prior to admission the patient began to have fairly profuse nosebleeds occurring two or three times weekly. These were not associated with other symptoms until one year ago, when she began to have frequent frontal headaches of varying severity which were often relieved by these nosebleeds. The latter did not change in frequency. At this time the catamenia, which had always been regular, suddenly ceased. A physician was consulted and he told the patient that she had high blood pressure. Six months before coming to the hospital the nosebleeds began to occur three to four times daily, and three months later she had puffiness of the face which lasted for about two weeks. Ready fatigue, dyspnea and palpitation on exertion, and listlessness became evident. During the preceding two weeks she was awakened at night several times by smothering sensations which caused her to cough. She occasionally expectorated a small amount of blood and twice vomited large amounts of yellowish fluid streaked with blood. The discomfort subsided after a brief period but was evidently not relieved by sitting up. Her appetite remained unimpaired and there was no note of weight change.

The past history is noncontributory.

Physical examination showed a well-developed and nourished pallid girl with an ammoniacal odor to her breath. The retinal arterioles were small and the discs were pale with somewhat hazy margins. There were no hemorrhages or exudate. A small amount of fresh blood was present within the nose. The heart was enlarged to the left and a blowing systolic murmur was heard at the apex. The blood pressure was 190/130. The lungs were clear and the remainder of the examination negative.

The temperature was 99°, the pulse 90. The respirations were 30.

Examination of the urine showed a maximum concentration of 1.014. There was a large trace of albumin and the sediment contained 8 to 10 white blood cells, 6 to 8 red blood cells, and a rare hyaline cast. A phenolsulphonephthalein test showed no excretion of dye at the end of one hour. The blood showed a red cell count of 2,660,000, with a hemoglobin of 40 per cent. The white cell count was 5,200, 75 per cent polymorphonuclears. The stools were negative. A Hinton test was negative. The nonprotein nitrogen of the blood was 130 milligrams and the plasma protein 5.1 grams. An electrocardiogram showed a late inversion of T_1 and a flat T_2 with small complexes. Lead IV was negative.

Plain films of the abdomen showed the faint shadows of rather small kidneys. There was no evidence of renal stone and the visualized bones appeared to be normal. A soft tissue mass in the left upper abdomen had the appearance of an enlarged spleen.

The patient was treated supportively and given a small transfusion. The nonprotein nitrogen rose to 175 milligrams and she was discharged for home care on the eighteenth hospital day.

Final Admission, eleven days later.

Following her discharge the patient became rapidly worse and developed orthopnea, edema of the legs, and drowsiness. She was brought to the hospital in a semiconscious state.

Physical examination showed a semicomatose patient with pallid dry skin and marked orthopnea. A few small hemorrhagic spots were noted in the skin and conjunctivae. The retina appeared edematous but no exudate was present. The chest showed dulness at both bases with increased tactile fremitus on the left. Many crackling râles were heard at the left apex anteriorly and throughout the left chest posteriorly. The heart was enlarged to the left and the sounds were pounding in character. The blood pressure was 175/120. There was pitting edema of the ankles.

The temperature was 101°, the pulse 130. The respirations were 25.

Examination of the urine was unchanged. The blood showed a red cell count of 1,870,000, with a hemoglobin of 40 per cent. The white cell count was 12,600, 89 per cent polymorphonuclears. The nonprotein nitrogen was 160 milligrams and the CO_2 combining power 36.9 volumes per cent.

The signs in the patient's chest gradually cleared up but her general condition remained critical. She developed occasional twitching and began to vomit frequently. The nonprotein nitrogen gradually rose to 270 milligrams. On the thirty-seventh hospital day she became comatose and died on the following day, about two months after her initial entry.

Differential Diagnosis

Dr. F. Dennette Adams: Recurrent persistent nosebleed, occurring in a girl of this age, if not caused by a local lesion, is due most likely to leukemia, purpura, or some other blood dyscrasia, or to active rheumatic infection or nephritis with hypertension. There are no symptoms in the history given at the first admission to suggest a primary blood disease, but there is sufficient evidence to justify a consideration of rheumatic heart disease, and much more in favor of chronic nephritis.

Acute pain in the abdomen in children, coming on suddenly with fever, nausea, vomiting, and systemic reactions, is frequently wrongly diagnosed acute appendicitis when actually due to early pyelitis or lobar pneumonia. The differential diagnosis is often difficult, for in the early stages, the child with pneumonia may have no signs in the lungs, and very early pyelitis may show a clear urine. It is usual for children with either disease to refer pain to the umbilical region or to one of the lower quadrants, so that in cases of right-sided lung or kidney infection an innocent appendix is often removed. Without going at length into the differential diagnosis, it might be worth while pointing out that as a general rule the child with appendicitis does not, at onset, appear so ill as the one with either of the other conditions; fever, tenderness, general systemic reactions in the former are not nearly so severe, nor is the leukocyte count so high. In fact, the child with an acute appendicitis is notorious for not seeming sick. The signs and symptoms are often mild, a circumstance which accounts for the relatively large number of cases of ruptured appendices in children.

The statement that following the pyelitis this patient was discharged cured is worth comment. A kidney, once infected, may harbor bacteria for years and develop an immunity to them, but recurrences of active infection can follow any additional burden put upon the individual by some other factor such as exposure, fatigue, pregnancy, or ureteral block.

The first symptom of the present illness (nosebleeds) appeared two years prior to admission. Four, three, and two years before the onset of the nosebleeds she had had severe attacks of sore throat. Here we have a possible etiologic factor for either nephritis or rheumatic infection. The presence of headaches is more suggestive of nephritis. The other symptoms mentioned could be accounted for by either disease, but with active rheumatic infection sufficient to cause as much trouble as this patient was experiencing, one would certainly expect that joint symptoms of a mild degree at least would have occurred at some time previously.

The fact that the patient's physician found high blood pressure favors the diagnosis of nephritis, but this evidence cannot be too strongly relied upon, since we are not given the systolic and diastolic levels. High systolic with high diastolic pressure would occur with nephritis; high systolic with low diastolic is a feature of insufficiency of the aortic valve due to rheumatic heart disease or syphilis.

The attack of nocturnal dyspnea, with hemoptysis, was most likely due to left ventricular failure. It could be associated with hypertension, with mitral stenosis or other type of valvular disease. Puffiness of the face is not seen in congestive failure except with generalized edema, and is therefore in this case a distinct piece of evidence in favor of chronic nephritis. If chronic nephritis is present, it is surprising that there should be no mention of nocturia, caused by the inability of the urine to concentrate, always an outstanding feature of the advanced case of chronic glomerulonephritis.

All things considered, there are more points in the history in favor of chronic glomerulonephritis than of any other condition.

The outstanding features of the physical examination were the pallor and the circulatory findings. Pallor can be a concomitant of almost any chronic disease; if true anemia were present we would be more suspicious of nephritis than of heart disease. The cardiac hypertrophy, and the high blood pressure, especially the high diastolic, point definitely toward nephritis. The systolic murmur at the apex is undoubtedly caused not by actual valvular disease but by relative insufficiency of the mitral valve due to hypertrophy and dilatation of the left ventricle.

The laboratory findings clinch the diagnosis. If the maximum concentration of 1.014 was determined by one of the concentration tests, we have evidence of severe kidney damage. The other findings are quite consistent. The failure to concentrate urine and to excrete the dye indicate marked kidney failure.

A Physician: What is the lower level of normal in the concentration test?

Dr. Adams: The test is done in this hospital by giving the patient nothing to eat or drink after 6 p. m., and collecting specimens at 6, 7 and 8 a. m. Some observers believe that if the test is performed in this manner the urine should show, in the second or third specimen, a concentration as high as 1.026, and that any-

thing lower than this indicates decreased function. One would prefer to repeat the test several times, however, before condemning a kidney which fails to show this high level of concentration. It is certainly safe to assume kidney damage if the gravity of the second or third specimen fails to exceed 1.016. A gravity fixed at 1.012 or lower indicates severe damage and impending uremia.

Secondary anemia is always present in advanced glomerulonephritis; hence the low erythrocyte count and hemoglobin.

A PHYSICIAN: How was the phenolsulphonephthalein test done?

DR. ADAMS: It was probably done intravenously, that being the present routine in this hospital. Specimens are collected fifteen minutes, a half hour, and an hour after injection. One expects, in the usual case, at least 25 per cent excretion in the first fifteen minutes, another 15 per cent in the second fifteen minutes, and a total of 50 per cent at the end of one hour.

A PHYSICIAN: Why do you use the intravenous rather than the intramuscular method?

DR. ADAMS: The intramuscular test is not so satisfactory, because in a case with edema, absorption of the dye from the arm may not take place.

DR. TRACY B. MALLORY: There is also another important point brought out by Dr. Earle Chapman. The speed of excretion is even more important than the total excretion at the end of one or two hours. This can be adequately determined only by the intravenous method and fractional determination as just described.

A PHYSICIAN: Is delay considered important?

DR. ADAMS: Yes. The most important part of the test is the determination of how much dye is excreted in the first fifteen minute specimen. Anything under 25 per cent is considered delay.

A PHYSICIAN: I get a little confused with nephritis and nephrosis. May we assume that true nephritis must have red cells in the urine?

DR. ADAMS: I think that depends upon how slow the process is. If the disease is progressing very slowly you may not find red cells unless a quantitative count is done on a twenty-four hour sediment. In the terminal stage of very slowly progressing nephritis you may not get red cells. If there is a more active process you do. The characteristic features of the nephrotic urine are large amounts of albumin and many casts, a large proportion of which are fatty. There are often mixed types which one cannot definitely classify.

DR. MALLORY: I shall read the actual record of successive urine specimens on different days. The figures on red cells are: 6 to 8, 4 to 6, 3 to 5, many, occasional, 2 to 7, 6 to 8. There was a constant, usually slight, occasionally fairly marked hematuria.

DR. ADAMS: The stools were negative. One would not be surprised to find a positive guaiac in a case of this kind. Terminal colitis with uremia is very common and might produce some blood in the stools. The nonprotein nitrogen figure indicates uremia. The plasma protein is somewhat low, as is usually the case with advanced nephritis. In nephrosis or chronic nephritis with edema it would be much lower.

I cannot explain the T wave changes and the low voltage in the electrocardiograms, unless there was pericardial effusion. This picture would fit coronary sclerosis; but one does not expect this condition at the age of nineteen. With a large heart and hypertension we would expect to have left axis deviation reported. Acute pericarditis, like colitis, is a common terminal event in uremia. If present, there might or might not be a friction rub.

The roentgen studies of the kidney were done doubtless to exclude hydronephrosis, stone, or secondary enlargement due to block from stone, kinked ureter, or some similar cause. The bones were x-rayed very probably to provide evidence for or against hyperparathyroidism. Stone in the kidney, bone softening, cyst formation, and nephritis are all important symptoms of this disease, and we are always on the lookout for it here. There is no evidence in this case. Enlargement of the spleen by x-ray could be explained on the basis of chronic passive congestion, although one usually finds the liver also enlarged.

The history, physical examination, and laboratory findings are all typical of chronic glomerulonephritis in the uremic stage. Whether this disease might be related in some way to the former attack of pyelitis and be the end-result of a slowly progressing pyelonephritis cannot be stated. One suspects that it might be, yet there is a past history of three severe attacks of tonsillitis; so it is just as possible that the tonsils might have served as the focus of infection, and the pyelitis have had no relation to the later disease of the kidneys.

A PHYSICIAN: How do you feel about transfusion in the treatment of this patient? It seems to me a rather radical procedure.

DR. ADAMS: They transfused in this case probably to bring up the red blood count and the serum protein.

A PHYSICIAN: As a general rule do they do that if they find severe anemia in nephritis?

DR. MALLORY: No, you can safely say that they do not.

DR. ADAMS: They transfuse nephrosis cases in an effort to bring up the serum protein. One

can imagine that transfusion was done in this case because the family may have demanded it.

The second admission followed discharge by only twelve days, yet the patient was distinctly worse. Orthopnea and edema indicate increased failure of the cardiorenal system; drowsiness, an increase in the degree of uremia.

The small hemorrhagic spots noted in the skin and conjunctivae are common in the terminal stages of nephritis and are another indication of downward progress. So is edema of the discs. One would expect to find retinal changes in the form of hemorrhages and exudates.

The chest signs are confusing, particularly if, since they are not mentioned, we must assume that the breath sounds are normal. Dulness at the bases in this case could be a sign of terminal pneumonia, or of pulmonary congestion, or beginning hydrothorax based on cardiac failure. The râles in the left chest posteriorly could be interpreted as due to congestion or pneumonia; those at the apex cannot be explained. Increased tactile fremitus does not occur without some changes in the breath sounds. It is a sign of pulmonary consolidation or compression. It could be due in this case to pneumonia, or to compression from fluid in the pericardial sac, associated with the terminal pericarditis mentioned earlier.

The cardiac signs are those of a laboring, hypertrophied, hypertensive heart.

There are three possible causes for the elevation of temperature: (1) terminal pneumonia, (2) terminal pericarditis, and (3) terminal colitis. The first can be associated with the final stages of almost any chronic disease; the two latter are peculiarly common in chronic nephritis. We have no direct evidence of any one of the three. Any of them could exist.

We have, then, the typical picture presented by the completed case of chronic glomerulonephritis, with hypertension, hypertrophy and dilatation of the heart, and uremia. Bronchopneumonia, terminal pericarditis, or colitis—one or all—could be present, and clinically should always be looked for in these cases. Fluid may or may not be present in one or both pleural cavities. It is often a feature of terminal nephritis with uremia and cardiac failure. There is no conclusive evidence in this case either for or against it. It is always unwise, in advance of autopsy, to guess at the size of the kidneys. If forced to commit myself on that point, however, I would anticipate small, granular, contracted kidneys. This would be my conjecture even if the roentgenologist had not reported small kidneys.

DR. MALLORY: What do you mean by "small" kidneys?

DR. ADAMS: The normal kidneys together weigh about 250-260 grams, do they not?

DR. MALLORY: Three hundred grams is usually considered low normal, but in a girl of this size that would be all right.

DR. ADAMS: Then I should say that the two together weigh about 100 grams. That, of course, is a wild guess.

A PHYSICIAN: Will you discuss further your reference to acute pericarditis?

DR. ADAMS: Fibrinous or serofibrinous pericarditis is a common complication of the later stages of chronic glomerulonephritis. Usually it occurs within the last week or so, but I have seen it two or three months in advance of death. Its presence should be suspected, and the rub typical of the condition should be sought in every case. We have no direct evidence in this patient, unless we consider the increased tactile fremitus over the left base as being due to compression of the lung by a large collection of pericardial fluid behind the heart. It is usually accompanied by considerable elevation of the temperature and leukocyte count. Because of its frequent occurrence and its not uncommon failure to manifest itself, one must also always consider acute colitis as a terminal possibility.

I am particularly interested in hearing what Dr. Mallory has to say concerning the etiology in this case. Was or was not the pyelitis a factor in the production of the nephritis?

A PHYSICIAN: Can you tell us anything about the creatinin in these patients—especially, its value as a diagnostic or prognostic aid?

DR. ADAMS: It more or less follows the trend of the nonprotein nitrogen, does it not?

DR. EDWARD A. GALL: It lags slightly behind the nonprotein nitrogen. It used to be said that a value of 6 to 8 milligrams represented a poor prognosis and signified a rapid course. However, currently we have seen cases with levels up to 11 to 12 milligrams, and they manage to drag along for months.

A PHYSICIAN: Have you ever found ammoniacal odor of value, or is it something one reads about and thinks ought to be there?

DR. ADAMS: These patients certainly have a uriniferous breath which can be detected readily and is very characteristic of the disease. It must not be confused, however, with the similar odor which emanates from beneath the bedcovers of a patient who is incontinent.

DR. F. DENNETTE ADAMS' DIAGNOSES

Chronic glomerulonephritis with hypertension and uremia.
Hypertrophy and dilatation of the heart.
Chronic passive congestion.
Serofibrinous pericarditis?
Acute colitis?
Bronchopneumonia?
Hydrothorax, bilateral?

Anatomic Diagnoses

Chronic glomerulonephritis.
Atrophy (pyelonephritic ?) of the left kidney.
Cardiac hypertrophy.
Hydropericardium.
Hydrothorax, bilateral.
Ascites.
Colitis, acute hemorrhagic.
Purpura.
Bronchopneumonia.

Pathologic Discussion

Dr. Mallory: The autopsy showed very much what Dr. Adams predicted. The pair of kidneys together weighed only 100 grams. It was interesting, however, that one of the kidneys was very much smaller than the other. We know there is a great deal of normal variation in the size of the kidneys and for that reason we commonly weigh them together rather than separately. One of these kidneys, however, weighed 80 grams and the other only 20. That seems rather more than could be considered a normal degree of variation on the two sides, although anything is possible down to a single kidney. The right kidney was the larger of the two, but of course it was nevertheless considerably smaller than normal. A normal kidney would weigh 150 grams. This weighed 80 grams, which is just about half the size. The capsules, as you would expect, stripped with a great deal of difficulty. In other words, there were adhesions between the capsules and the renal tissue, as there always are when scar tissue has formed in the kidney substance. When the capsules finally were stripped they left scarred granular surfaces and the general color was rather yellowish, which would suggest that significant amounts of fat were present, probably a fatty degeneration. The calices were somewhat dilated and the pelvic fat increased. Grossly there was no definite evidence of pyelonephritis. Another gross finding was, of course, hypertrophy of the heart, which weighed 450 grams. The normal for her would probably have been 300 grams; so that it is considerably hypertrophied and that hypertrophy, as you would expect, was almost entirely in the left ventricle, undoubtedly secondary to the hypertension. The left ventricle measured 22 millimeters, whereas the normal usually is about 14 millimeters. The right ventricle was a little hypertrophied, measuring 5 millimeters, as against the normal of 3 millimeters. The liver was normal in size. The spleen was moderately enlarged, weighing 330 grams. That was about twice the normal size but is still below the limit of palpability. You very seldom feel a spleen that does not weigh 400 grams or more. The pericardium contained about 500 cubic centimeters of clear fluid. There was no fibrin at all; in other words the terminal pericarditis that is almost a standard complication of uremia was not present here. How long that pericardial fluid had been there, there is no possibility of saying. We have seen occasional cases with negative chest plates taken within twenty-four hours of death that come to autopsy with a liter of fluid in the pericardium, and more than a liter in each of the chests, so tremendous amounts of fluid can accumulate in the serous cavities of the thorax in a very short period of time. It may all have appeared in the last twenty-four hours of life or may have been present for two or three weeks and may have accounted for some of the physical signs, as Dr. Adams suggested. The pleural cavities contained relatively little fluid and the lungs were markedly edematous and that lower lobe on the left, where the questionable signs were, showed a little more fluid than elsewhere, some collapse and very numerous focal hemorrhages. Hemorrhages similar to those which were seen in the skin were present in a great many of the organs, in the pericardium and on the pleural surfaces. There were scattered hemorrhages throughout the lung and very marked hemorrhage with some slight degree of ulceration in the colon; in other words, a terminal uremic colitis. It is a very rare case of nephritis dying in uremia that does not show either pericarditis or colitis. A great many show both. What they are due to we have not the faintest idea. The pericarditis is always sterile. It is apt to be present in the patient in the uremic state, regardless of whether the nonprotein nitrogen is 85 or 300. You may see it in uremia with a nonprotein nitrogen of 85 and it may not be present in a uremia with a nonprotein nitrogen of 300. It seems unlikely that it is directly due to nitrogen retention. There was one other finding that we are beginning to discover is very characteristic in cases of long-standing renal insufficiency which Dr. Adams did not mention and which we would not have thought of looking for a year ago. There is a quite close relationship between the parathyroids and renal insufficiency and if renal insufficiency is fairly chronic, that is if it has lasted more than a year, you can pretty regularly count on parathyroid enlargement. Usually it is relatively slight. In this case all four of the parathyroid glands were enlarged and the total weight of the parathyroid tissue was .6 grams. Normally each parathyroid weighs 30 milligrams and the total weight is a little over .1 gram. These are nearly five times the normal size. On the other hand we have seen two nephritics here, and several have been reported from other places, in which parathyroid tissue weighing as much as 5 or 10 grams has been

found and those cases may begin to show all the clinical evidences of hyperparathyroidism including the formation of bone cysts. This patient had a single blood phosphorus done with this idea in mind just before death which was 15 as against the normal of 2.

The question that particularly interests pathologists in this sort of case is what kind of nephritis we are dealing with and there you get on very questionable ground. The commonest type of renal pathology leading to prolonged renal insufficiency in a young person is, of course, chronic glomerulonephritis and that is the first thing to think of here. The question of whether we have not too easily accepted all these cases as chronic glomerulonephritis has recently been raised, particularly by Dr. Longcope at the Johns Hopkins Hospital. Some of you very possibly have seen his articles. He feels that a quite significant number of cases of chronic renal insufficiency in young individuals are due to a long-standing "burnt-out" pyelonephritis rather than to glomerulonephritis. I have very little doubt he would immediately seize upon this case as evidence in support of his theory. In many of these cases you cannot get any history of pyelitis but that does not rule it out, because often the chronic type of disease causes very few symptoms unless from time to time it dams up and you get fever. It is perfectly possible for pyelitis to run for years and produce a great deal of damage without attacks of chills and fever. This girl we know had a fairly severe pyelitis at one time. And to go with that we have one markedly atrophied kidney. The microscopic sections of the smaller kidney showed a good deal of lymphocytic infiltration beneath the pelvic epithelium. It is very possible and I think probable that she had a rather severe pyelonephritis on that side. The other kidney, however, does not suggest it at all and looks like the typical end stage of chronic glomerulonephritis. So that I would be inclined to guess in this case that she had a double lesion, that she had a chronic glomerulonephritis and a pyelonephritis, which was localized to one side, and produced extensive atrophy of one kidney, in that way throwing a greater burden on the other kidney and speeding up the development of renal insufficiency.

A Physician: Is it possible she might have had the original attack of pain from an impacted stone even though the stone could not be demonstrated?

Dr. Mallory: It is conceivable. We did not find any stones at autopsy. If she had had one it must have been passed. You do not have to have a stone to have a good deal of pain because pyelitis alone can cause it.

Dr. Adams: Did you account for the enlargement of the spleen except by chronic passive congestion?

Dr. Mallory: I admit it is a somewhat inadequate explanation. It does not satisfy me because the liver was not quite so large as you would expect with passive congestion.

Dr. Adams: There was very little passive congestion in the lungs by x-ray even back to the first admission.

A Physician: Does the converse hold with parathyroid disease even of mild degree when chronic nephritis develops?

Dr. Mallory: Yes and no. There is always the possibility of developing secondary renal insufficiency in parathyroidism but it is directly due to one factor, that the large amounts of calcium that are excreted lead to the precipitation of calcium phosphate in the renal passages. The common thing to find is an ordinary renal stone in the pelvis. The majority of our parathyroid cases we have picked up by routinely hunting for hyperparathyroidism in all cases coming to the hospital because of stones. On the other hand, there is a group of cases or perhaps a stage in the disease in which the calcium is precipitated before it reaches the renal pelvis, in the renal tubules themselves, and in that way calcium can be precipitated throughout the kidneys. Kidneys of that sort show up beautifully by x-ray and here we know there was no evidence of that. You can see the faint kidney outline that you often see in a flat plate but had they been calcified they would have stood out almost as clearly as bones do. It takes a very severe and very prolonged hyperparathyroidism in general to damage the kidneys seriously. The marked cases that we have seen have given histories of at least ten years' duration.

CASE 22342

Presentation of Case

An eighteen day old Negro boy was admitted to the Massachusetts Eye and Ear Infirmary with a purulent discharge from both eyes.

The father and mother were living and well. There were two siblings, ages three and a half and one and a half years, living and well. There was no family history of tuberculosis.

The child had been born on the maternity ward of a neighboring hospital. The usual prophylactic treatment had been given to the child's eyes at birth. At the age of twelve days the eyes began to show a slight discharge. This did not seem disturbing and the child was discharged home with the mother at the age of sixteen days.

At home, however, the eyes began to show a marked discharge and the child was brought to the Eye and Ear Infirmary by a visiting nurse. He was admitted to the ward. No gonococci were found on the smear.

The child's temperature on admission was 101.5°. It fell to normal on the third day in the hospital but on the fifth day it again became elevated and except for a period of two days the temperature was between 100° and 101° during his eleven days' stay at the Infirmary. The eyes responded to treatment very satisfactorily and seven days after admission were well. With the second rise of temperature the child began to show signs of a respiratory infection—a cough and a running nose. Râles were heard over the chest. An x-ray picture revealed some pulmonary infiltration. On the eleventh day in the hospital, when the child was twenty-nine days old, he was transferred to the Children's Medical Service at the Massachusetts General Hospital.

On admission to the General Hospital, the patient had a mucoid nasal discharge, a slightly injected throat, an occasional dry cough, and medium crepitant râles over the left back and axilla, with questionable dulness over this area. The heart was normal. The eyes were clear. The temperature was 98°, rose to 102° on the second day, but remained below 100° thereafter throughout his stay in the hospital.

No abnormalities were found on examination of the urine or stool. The blood showed a white cell count of 16,200, 37 per cent polymorphonuclears, 55 lymphocytes, 5 monocytes, and 1 eosinophil; the count rose to 35,000 two weeks later with 60 per cent polymorphonuclears, 38 lymphocytes, and 2 monocytes. The red cell count was 4,200,000, with a hemoglobin of 75 per cent. The red cells and platelets were normal in appearance. A tuberculin test 1:100 intradermally was negative.

The patient's general condition showed little change during the next three weeks. He had frequent troublesome coughing spells; the cough did not clear up with codein and expectorants. Râles were heard on both sides of his chest, especially on the left side. Probable dulness was present over both bases. He frequently had a mucopurulent discharge from his nose for which he was given, over a period of fourteen days, nose drops containing neosilvol and ephedrin, but no albolene. His pulse varied between 120 and 170 and his respirations between 40 and 80. The temperature was normal. The child did not eat very well but maintained his weight. He did not vomit his feedings. X-ray examination two weeks after admission showed mottled dulness throughout both lung fields from apex to base. Three days later another film showed very much the same appearance except that the costophrenic angle was obliterated on the right. On the day before the child died his temperature fell for a few hours to between 96° and 97°. Death occurred suddenly and unexpectedly, the child being found dead in bed; this was on the thirty-third day after his admission to the Eye and Ear Infirmary.

Differential Diagnosis

Dr. R. S. Eustis: The discharge from the eyes does not sound like a gonorrheal ophthalmia. There is no mention of examination of smears from the discharge. They should have been made and presumably were made and found to be negative. It is too late for a gonorrheal ophthalmia to flare up from infection at the time of delivery. If the child had been cared for at home it is possible that there might have been infection from the hands of the nurse; but I do not believe that is likely to occur in the hospital.

From the fact that the child was admitted to the ward I assume that the eyelids were pretty well swollen and they felt they could not get adequate drainage treating him as an outpatient.

No gonococci were found in the smear on entry to the Eye and Ear Infirmary. I believe that pretty well rules out a gonorrheal ophthalmia. We must remember, however, that there are many cases of nongonorrheal ophthalmia that are just about as severe as the gonorrheal variety.

The child's temperature on admission was 101.5°. My impression is that the condition of the eyes was probably not severe enough to account for that, and yet there is no mention in this record of any other infected area. Then the temperature comes back to normal, so that perhaps the eyes were causing it, as they improved rapidly under frequent irrigations.

At the time of transfer to the Massachusetts General Hospital I believe that he had an upper respiratory infection. Whether he had brought it into the Infirmary with him or whether he had caught it from some of the attendants at the Infirmary, I do not know. Upper respiratory infection in a newborn baby is a serious condition. It is very apt to extend down as this baby's infection extended down, causing bronchitis, and a bronchitis that lasts more than a day or so in a baby is a bronchopneumonia. I feel that at the time of admission to the Massachusetts General Hospital, even though the x-ray showed only a little pulmonary infiltration, the baby probably had both an upper respiratory infection and bronchopneumonia.

A normal temperature and the absence of bronchial breathing and dulness are compatible with the presence of bronchopneumonia during the newborn period. The first blood examination is normal for a three weeks' old baby. Two weeks later the white blood count rose to 35,000 with 60 per cent polymorphonuclears. This confirms the presence of infection

and suggests the possibility of there being pus somewhere. We have no localizing symptoms as yet except the symptom of cough and the signs of bronchitis.

The negative tuberculin test does not rule out tuberculosis. A positive test would be important but the negative test means nothing. If the child has tuberculosis it must be an active process.

The patient's general condition showed little change during the next three weeks. He had frequent troublesome coughing spells. The cough did not clear up after codein. Did it suggest whooping cough?

DR. HAROLD L. HIGGINS: It used to come in bouts.

DR. EUSTIS: I do not think he had whooping cough. I have seen these cases of bronchopneumonia in the newborn with cough that sounded very much like whooping cough, possibly due to enlarged bronchial glands. Usually it is due to the presence of mucus in the trachea. Such a baby is weak, is lying on his back, is helpless, and has spasmodic cough.

They note particularly that there was no albolene in the nosedrops, because inhalation of oily fluids given for the treatment of nasopharyngitis may result in oily deposits through the lung which cause permanent damage and not, uncommonly, death. However, it is perfectly possible that even watery solutions, if given too generously, might get into the windpipe of a weak infant and cause irritation and cough.

The rapid respiratory rate bears out the diagnosis of pulmonary infection.

He did not vomit. That is another important note, because vomitus may be inhaled by a weak infant and cause an inhalation pneumonia.

Is this mottled dulness in the x-ray bronchopneumonia, or is it the mottled dulness of miliary tuberculosis? He certainly has pulmonary pathology but I do not think that pulmonary pathology is tuberculosis, do you Dr. Hampton?

DR. AUBREY O. HAMPTON: This film shows a small fairly dull right upper lobe and what looks like enlarged glands at the right lung root. There is also density at the right base and at the left apex. The remainder of the left lung is fairly clear. The heart has shifted toward the right at this examination and I think the upper lobe is reduced in size. At the next examination the changes on the right have decreased somewhat but he now has a fairly diffuse process on the left side. This last film shows clearing in the upper lobe apparently. There is very little change in the remainder of the lung except that now he has a diffuse pleural effusion on the right side. This film at the first examination alone is not inconsistent with tuberculosis. He is three weeks old or thereabouts. We can say that he has congenital atelectasis of the upper lobe and infection in the lung. While in the hospital this atelectatic upper lobe expands but the infection progresses.

DR. EUSTIS: How do you explain this flattening of the costophrenic angles?

DR. HAMPTON: It looks like a thin layer of free fluid that extends from the apex to the base. He is lying on his back.

DR. EUSTIS: I do not believe he has tuberculosis. I think he has a descending infection from a head cold that he might have acquired at home or may possibly have picked up the first day or so in the Eye and Ear Infirmary. He came in without mention of head cold. We have evidence of enlarged bronchial glands that I mentioned in connection with paroxysmal cough, bronchopneumonia and some terminal complication. He had fluid in the right chest by x-ray. The question is, Was that fluid serous or purulent? In favor of its being an empyema is the high white count. There was not enough fluid there to kill him suddenly. There was no mention of displacement of the heart to the left but I think a young infant can perfectly well die suddenly from an empyema. There is also another possibility that during the last few days he may have developed a pericarditis. That is not an uncommon cause of sudden death in infancy and I suspect that may have been the case here, as such pericardial effusions in infancy are almost impossible to diagnose during life.

DR. HAROLD L. HIGGINS: There were certain things about this case that made us think of whooping cough. In the first place he had a fairly normal temperature, paroxysms of coughing, a bronchitis which started as a common cold, and then he died quite suddenly. A baby under six months when he gets whooping cough may get a spasm of the larynx and die in it although he may never have whooped at all. These whooping cough patients usually have been seen in several such spasms, in which they cannot breathe and get cyanotic, before one occurs in which they die. Our patient was not exposed to whooping cough at home. He was at home only two days, and there has been no whooping cough in the hospital. There was an epidemic of bronchitis in the city: very often bronchitis can give symptoms similar to whooping cough.

One has to think of lipopneumonia. Although he did not get albolene, I believe he did get cod liver oil, as all the babies at the Infirmary do. I think of this as a possibility although not as likely.

Of course tuberculosis was thought of by the staff, and also the possibility of aspiration of food and then again the possibility of upper respiratory infection which extended down to form a bronchopneumonia. About one-third of

the children with ophthalmia neonatorum that come to the Eye and Ear Infirmary have a gonococcus infection. In the other two-thirds no gonococci are found; some of them have pneumococcus infections of the eyes. The pneumococcus infection in his lungs, with bronchitis and bronchopneumonia, may have been secondary to the eye infection.

Clinical Diagnosis

Bronchopneumonia.

Dr. R. S. Eustis's Diagnosis

Ophthalmia neonatorum (nongonorrheal).
Nasopharyngitis.
Bronchopneumonia.
Empyema?
Pericarditis?

Anatomic Diagnoses

Streptococcus bronchopneumonia.

Pathologic Discussion

Dr. Tracy B. Mallory: The x-ray examination I think was responsible for one misinterpretation here. The child had no fluid in the lungs but had marked pleural adhesions. Both pleural cavities were absolutely dry. There was an extremely extensive bronchitis and bronchiolitis running down to the most terminal branches of the tree. There was a moderate amount of pneumonia but a good deal more collapse. That is very characteristic of bronchopneumonia as one sees it in infants. The bronchi are usually very widely involved and the changes in the lung are rather more those of atelectasis than consolidation. There were, however, in this case, numerous dilated alveoli filled with exudate as well. Cultures from the lungs and the heart blood showed streptococci, both hemolytic and nonhemolytic. We did not find pneumococci. The question as to whether it might have been whooping cough, I think the postmortem fails to answer. It is perfectly conceivable that it could have been. We did not make cultures direct from the bronchi for pertussis organism and the microscopic picture of the lungs is not distinct enough to make the diagnosis.

A Physician: How about lipopneumonia?

Dr. Mallory: There was none.

The New England
Journal of Medicine

SUCCESSOR TO
THE BOSTON MEDICAL AND SURGICAL JOURNAL

Established in 1828

Published by THE MASSACHUSETTS MEDICAL SOCIETY under the jurisdiction of the

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Material for early publication should be received not later than noon on Saturday. Orders for reprints must be sent to the Journal office, 8 Fenway.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to The New England Journal of Medicine, 8 Fenway, Boston, Mass.

MEDICAL SCIENCE FOR THE LAYMAN

AN increasing number of articles dealing with the modern advances of science is constantly appearing in the daily press, and one cannot fail to be impressed with the improvement in the quality and accuracy of such reports. This improvement is due, in a large part, to the reprinting of material released by *Science Service*, a nonprofit institution in Washington founded in 1921 for the express purpose of making available to the general public short, simply worded, accurate and interesting accounts of scientific advances. Its work is supervised by a board of trustees nominated by the National Academy of Sciences, the National Research Council, the American Association for the Advancement of Science, the E. W. Scripps Estate and the journalistic profession. This agency is to be congratulated for fulfilling its function so well, particularly in matters concerning the more exact sciences, such as astronomy, physics and chemistry.

With the biologic sciences the value of such abstracts is often questionable, particularly in those dealing with the science of medicine. In spite of the accurateness of the original résumé, it is frequently falsely interpreted either by the staff of the newspaper or by the readers. Either or both fail to realize that medicine is one of the less exact sciences, that the claims of one man or one group must be confirmed by many others before they can be accepted, that experimental findings have numerous limitations and that many fundamentally important contributions have, at the moment, little, if any, practical application.

Why falsely raise the hopes of a cancer-fearful public by reporting an alleged cancer cure, when it is well-known to all physicians that any cure based on an observation period of less than five years is open to doubt? Why capitalize on the observed experimental fact that a suspension in the air of the virus of influenza can be killed by ultraviolet light rays, when any attempt, at the moment, to apply the observation to the control of the disease is obviously futile? Or, why suggest that all postoperative infection may be eliminated by sterilizing the air of the operating room with the same ultraviolet light rays, when it is well known to the majority of surgeons that the simplest way to guard against air-borne infection is to be sure that no individuals harboring hemolytic streptococci in their noses or throats are included on the operating team?

When papers are read before a group of medical men, the authors realize that their audience is fully aware of the necessary limitations and will interpret the findings accordingly. Such is not the case with the reading public and one cannot help but comment on the desirability of more reserved newspaper reporting of papers dealing with the medical sciences.

THE REDUCTION OF NEONATAL MORTALITY

DR. CHARLES F. WILINSKY, Deputy Commissioner of Public Health of Boston, has been reported to have said that "premature birth is the chief cause of mortality under one year of age". This opinion seems to be substantiated by the fact that, of the fifty babies of each thousand born in Boston who die in the first year of life, from thirty to thirty-five die during the first two weeks of life.

Boston already has shown a marked reduction in the infant mortality rate which was eighty-four out of every thousand in the first year of life in 1926. This rate has been reduced to about fifty at the present time. It is reasonable to expect that progress will follow proper care of those born prematurely if modern methods of treatment are more generally adopted.

Dr. Wilinsky's purpose is to follow the plan now in operation in Chicago where infants born prematurely are placed in a heated incubator and promptly sent to well-equipped centers where constant medical and nursing care is available. In order to assure the likelihood of survival of these babies legislation should be adopted requiring the transfer of such cases to approved institutions, or the utilization of an incubator under the expert medical and nursing care plan. In furtherance of this object there is recommended more general attendance, particularly by those unable to avail themselves of the services of a private physician at the eighteen baby clinics in Boston, of mothers with these babies for instruction in the details of intelligent care of infants in the early weeks of life. These combined plans warrant a very reasonable expectation of a material reduction in mortality rates among children in the first year of life.

The assistance of the family doctor is especially indicated, both in his repeated examinations of infants in early life and in securing the co-operation of parents, when indicated, with the great importance of having premature babies cared for according to Dr. Wilinsky's proposed plan.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

THURMON, FRANCIS M. B.S., M.D. Harvard University Medical School 1926. Physician-in-Chief of the Clinic of Dermatology and Syphilology, The Boston Dispensary. Assistant Professor of Dermatology and Syphilis, Tufts College Medical School. Consulting Dermatologist, Boston Floating Hospital. Consultant, Tumor Clinic, The Boston Dispensary. His subject is Bismuth Ethyl Camphorate. Clinical Observations on a New Oil Soluble Bismuth in the Treatment of Syphilis. Page 315. Address: 520 Commonwealth Avenue, Boston.

SWARTZ, J. H. M.D. Harvard University Medical School 1920. Instructor in Dermatology, Harvard University Medical School. Member, American Dermatological Association. Assistant Dermatologist, Massachusetts General Hospital. Visiting Dermatologist, Beth Israel Hospital. Consulting Dermatologist, Massachusetts Eye and Ear Infirmary and Boston Psychopathic Hospital. His subject is The Rôle of Fungi in Medicine. Page 322. Address: 371 Commonwealth Avenue, Boston.

SULZBERGER, MARION B. M.D. University of Zurich 1926. Assistant Professor of Clinical Dermatology and Syphilology, New York Post-Graduate Medical School of Columbia University. His subject is Remarks on Definitions and Classification in Certain Forms of Dermatologic Allergy. Page 330. Address: 962 Park Avenue, New York City.

SULLIVAN, EDWARD COPPINGER. M.D. Harvard University Medical School 1903. Director, Venereal Disease Clinic, Springfield Hospital. His subject is The Doctor and Early Syphilis. Page 336. Address: 1597 Main Street, Springfield, Mass.

ABBOTT, CLIFTON S. M.D. Dartmouth Medical School 1894. F.A.C.S. Formerly President, New Hampshire Medical Society. Surgeon, Laconia Hospital. His subject is The President's Address. Page 342. Address: 507 Main Street, Laconia, N. H.

SHIELDS, J. DUNBAR. B.S., M.D. Tulane University of Louisiana School of Medicine 1931. Member of Medical Staff, Margaret Pillsbury General Hospital, Concord, N. H. His subject is The Irritable Colon: Diagnosis and Treatment by the General Practitioner. Page 344. Address: 4 No. State Street, Concord, N. H.

MISCELLANY

DR. W. R. MacAUSLAND'S APPOINTMENT AND THAT OF DR. A. R. MacAUSLAND

Governor Curley has appointed Dr. William Russell MacAusland to the position of member of the board of trustees of the Massachusetts State School for Crippled Children at Canton. Dr. MacAusland takes the position made vacant by the death of Mr. Walter C. Baylies. Other positions held by Dr. MacAusland are trustee and medical director of the Berkshire School for Crippled Children at Pittsfield, trustee of the Balch Hospital for Crippled Children at Manchester, New Hampshire, and director and trustee of the Sol-e-Mar convalescent hospital at South Dartmouth.

Dr. W. R. MacAusland and his brother, Dr. Andrew R. MacAusland, were recently appointed to the Staff of the Tufts College Medical School as Clinical Professors of Orthopedic Surgery.

THE MEDICAL DIRECTOR OF THE UNITED STATES QUARANTINE STATION, BOSTON HARBOR

Medical Director H. J. Warner of the United States Public Health Service has been directed to assume charge of the Quarantine Station at Gallops Island, Boston Harbor, on or about October 10, 1936. He will fill the position made vacant by the transfer of Passed Assistant Surgeon A. J. Aselmeyer to another position.

CORRESPONDENCE

THE USE OF QUINIDINE—AN EXPLANATION

Editor, *New England Journal of Medicine,*

In the review in the *Journal* of June 18, page 1271, of my book, "The Diagnosis and Treatment of Diseases of the Heart," occur these words, "It would seem unwise to recommend intravenous quinidine to the general practitioner without an added word of warning as to its danger." As this might create the idea that I advise that quinidine be given intravenously, it seems worthwhile to state that quinidine is indexed in this book as being discussed in relation to five varieties of cardiac disturbance; in all except one, of these mouth dosage is advised; there is considerable discussion of the dangers from quinidine even when given by mouth. In only one condition, paroxysmal ventricular tachycardia, is other than mouth dosage mentioned and then only in the following words: "It would seem wise to give the first dose intravenously using 0.2 to 0.3 gm." I trust this rather unfortunate statement of the reviewer will not lead any general practitioner on my supposed advice to use quinidine other than by mouth except as suggested in the last quoted sentence.

To follow my advice: "On the whole, alcoholic beverages seem to me to be inimicable for the patient with angina" will not, in my judgment, harm many, if any, patients.

To consider abnormal deposits of glycogen in the muscle as a variety of "congenital idiopathic hypertrophy" of the heart seems hardly in accord with my idea of a proper terminology.

Yours truly,

HENRY A. CHRISTIAN, M.D.

REPLY TO DR. CHRISTIAN'S LETTER*

There is no essential difference of opinion in the views of Dr. Christian and the reviewer so far as the use of quinidine is concerned, and it is worth noting that Dr. Christian says on page 297, "I have witnessed fatalities, which have given me a very healthy respect for the dangers of quinidine sulphate therapy." The impression given by Dr. Christian, so far as ventricular paroxysmal tachycardia is concerned, is that it always accompanies very serious cardiac conditions and, as such, requires "prompt and thorough" treatment. While this is usually true, in occasional cases it seems to carry no more serious prognostic implications than does auricular paroxysmal tachycardia. It, therefore, seemed not inappropriate to comment on the suggestion that, in ventricular paroxysmal tachycardia, "it would seem wise to give the first dose [of quinidine sulphate] intravenously, using 0.2 to 0.3 gram," because of the even greater danger of the drug by this than by the oral route.

So far as the use of alcoholic beverages in the treatment of angina is concerned, omission of them will not harm many patients, but in some, alcohol is distinctly beneficial and the reviewer's experience of its value would coincide more nearly with that of Heberden in his original description of angina, 150 years ago.

The etiology of congenital idiopathic hypertrophy of the heart is unsolved. If recent work showing that it may be related at times to abnormal glycogen deposits in heart muscle is to lead to more accurate classification of related syndromes, it seems fair to mention it if only to suggest to those having opportunity to study such cases pathologically, the possibility of finding it by special staining methods.

*By the Reviewer.

RECENT DEATHS

DODGE—WILLIAM WOOLDREDGE DODGE, M.D., aged 79, a retired physician of Hamilton, Massachusetts, died at the Beverly Hospital, August 11, 1936, after a long illness.

Dr. Dodge was born in Marblehead, was educated in the public schools and was a graduate of Tufts College and the Medical School of Harvard University.

He joined the Massachusetts Medical Society in 1886 and retired in 1924. He was also a Fellow of the American Medical Association. During his active years he practiced in Boston.

GOVE—WILFRED FREEMAN GOVE, M.D., of 15 Sawyer Street, Wareham, Massachusetts, died June 26, 1936. Dr. Gove was born in 1895 and graduated from the Boston University School of Medicine in 1926. He joined the Massachusetts Medical Society in 1927 and was also a Fellow of the American Medical Association.

NOTICE

UNITED STATES CIVIL SERVICE EXAMINATIONS

Senior Public Health Nursing Consultant, $4,600 a Year

Public Health Nursing Consultant, $3,800 a Year

Associate Public Health Nursing Consultant, $3,200 a Year

Assistant Public Health Nursing Consultant, $2,600 a Year

Public Health Nursing Assistant, $2,000 a Year

Applications must be on file with the United States Civil Service Commission at Washington, D. C., not later than August 31, 1936.

NOTICE OF MEETING

WORCESTER DISTRICT MEDICAL SOCIETY

CHANGES IN SCHEDULE 1936-1937

The meeting scheduled for September 16 has been postponed to September 23. The speakers for this meeting will be Dr. Richard Miller and Dr. Cadis Phipps of Boston, who will give a symposium on Peptic Ulcer, with Dr. Miller discussing the surgi-

cal aspects and Dr. Phipps the medical aspects of this condition.

Thursday afternoon, November 5, at 4:30, in the rooms of the Worcester Medical Library, Inc., at 34 Elm Street, Worcester, will be held the fall Censors' meeting.

Thursday afternoon, May 6, 1937, at 4:30 in the rooms of the Worcester Medical Library, Inc., at 34 Elm Street, Worcester, will be held the spring meeting of the Board of Censors.

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, AUGUST 24, 1936

Saturday, August 29—

*10 a. m. - 12 m. Staff Rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Reginald Fitz.

*Open to the medical profession.

August 24-29—Harvard University Tercentenary Celebration. See page 1166, issue of June 4. School of Public Health, page 310, issue of August 13.

September 4 to 8—First Congress of the Austrian Society for the Study of Roentgenology. For details address: Allgemeines Krankenhaus, Alserstrasse 4, Wien, IX, before September 1.

September 7, 8, and 9—The Cancer Institute. See page 309, issue of August 13.

September 7-10—International Union against Tuberculosis. See page 554, issue of March 12.

September 7-11—American Congress of Physical Therapy will meet at the Waldorf-Astoria, New York City. See page 52, issue of July 2.

September 9 to 12—Sixth Congress of the International Society for Urology. For details address Dr. Theodor Hryntschak, Rathausstrasse 3, Wien, I.

September 14 and 15—Tercentenary Session of the Harvard Medical School. See page 1166, issue of June 4.

September 16-21—First International Congress of Sanatoria and Private Nursing Homes. See page 803, issue of April 16, and page 264, issue of August 6.

September 22, 23, 24—Twelfth Clinical Congress of the Connecticut State Medical Society. See page 217, issue of July 30.

October 12-18—Third International Congress on Malaria. See page 1076, issue of May 21.

October 19-23—Clinical Congress of the American College of Surgeons. See page 180, issue of January 23.

October 19-31—1936 Graduate Fortnight of the New York Academy of Medicine. See page 1221, issue of June 11.

October 20-22—Academy of Physical Medicine, Annual Meeting, Hotel Statler, Boston.

October 20-23—The American Public Health Association. See page 1226, issue of June 11.

March 30 - April 2, 1937—First International Conference on Fever Therapy. Postponement notice. See page 52, issue of July 2.

April 21-24, 1937—American Society for Experimental Pathology. See page 1075, issue of May 21.

DISTRICT MEDICAL SOCIETY

WORCESTER DISTRICT MEDICAL SOCIETY

September 23, 1936 - May 12, 1937—See page 312, issue of August 13, and page 363 of this issue.

BOOKS RECEIVED FOR REVIEW

Passive Vascular Exercises and the Conservative Management of Obliterative Arterial Diseases of the Extremities. Louis G. Herrmann. 288 pp. Philadelphia and London: J. B. Lippincott Company.

Diseases of the Respiratory Tract. Eighth Annual Graduate Fortnight of the New York Academy of Medicine. J. Burns Amberson, Jr., George Blumer, et al. 418 pp. Philadelphia and London: W. B. Saunders Company.

The International Medical Annual. A Year Book of Treatment and Practitioner's Index. Edited by H. Letheby Tidy and A. Rendle Short. 555 pp. Baltimore: William Wood & Company. $6.00.

Collected Writings. Alfred F. Hess. Volumes I and II. 719 pp. and 734 pp. Springfield and Baltimore: Charles C Thomas. $15.00.

The Extra-Ocular Muscles. A Clinical Study of Normal and Abnormal Ocular Motility. Luther C. Peter. 351 pp. Second Edition. Philadelphia: Lea & Febiger. $4.50.

Sex and the Love Impulse. An Outspoken Guide to Happy Marriage. J. H. Burns. 61 pp. New York: Emerson Books, Inc. 50c.

Illustrious Contributors to Public Health. Charles Frederick Bolduan. 33 pp. Privately printed. 1936.

Food, Fitness and Figure. Jacob Buckstein. 252 pp. New York: Emerson Books, Inc. $2.00.

Principles and Practice of Recreational Therapy for the Mentally Ill. John Eisele Davis. In collaboration with William Rush Dunton, Jr. 206 pp. New York: A. S. Barnes & Company. $3.00.

The Patient and the Weather. Volume I. Part 2. William F. Petersen and Margaret E. Milliken. 781 pp. Ann Arbor: Edwards Brothers, Inc. $9.00.

Security Against Sickness: A Study of Health Insurance. I. S. Falk. 423 pp. New York: Doubleday, Doran & Company, Inc. $4.00.

International Clinics. Edited by Louis Hamman. Volume II. Forty-Sixth Series, 1936. 327 pp. Philadelphia, Montreal, London: J. B. Lippincott Company.

Syphilis and Its Treatment. William A. Hinton. 321 pp. New York: The Macmillan Company. $3.50.

Collected Papers of the Mayo Clinic and The Mayo Foundation. Volume 27. Edited by Richard M. Hewitt, Lloyd G. Potter, and A. B. Nevling. 1353 pp. Philadelphia and London: W. B. Saunders Company. $12.00.

The Study of Anatomy. Written for the Medical Student. S. E. Whitnall. Third Edition. 113 pp. Baltimore: William Wood & Company. $1.75.

Diseases of the Nose, Throat and Ear. For Practitioners and Students. Edited by A. Logan Turner and others. Fourth Edition, Revised and Enlarged. 473 pp. Baltimore: William Wood & Company. $6.00.

A Textbook of Histology. Joseph Krafka, Jr. 246 pp. Baltimore: The Williams & Wilkins Company. $2.50.

Urology in Women. A Handbook of Urinary Diseases in the Female Sex. E. Catherine Lewis. Second Edition. 100 pp. Baltimore: William Wood & Company. $2.25.

On Percussion of the Chest. Being a Translation of Auenbrugger's Original Treatise. John Forbes. 31 pp. Baltimore: The Johns Hopkins Press. 75c.

Synopsis of Diseases of the Heart and Arteries. George R. Herrmann. 344 pp. St. Louis: The C. V. Mosby Company. $4.00.

Exophthalmic Goiter and Its Medical Treatment. Israel Bram. 456 pp. Second Edition, Completely Revised and Enlarged. St. Louis: The C. V. Mosby Company. $6.00.

Proceedings of the Twenty-Fifth, Twenty-Sixth, Twenty-Seventh and Twenty-Eighth Conferences of the American Association of Medical Milk Commissions, Inc. 363 pp.

League of Nations. Quarterly Bulletin of the Health Organization. Volume V, No. 1, March 1936. 209 pp. 65c.

Medical Science Exhibits. A Century of Progress. Eben J. Carey. 204 pp. $2.00.

BOOK REVIEWS

An Index of Differential Diagnosis of Main Symptoms by Various Writers. Edited by Herbert French. Fifth Edition. 1145 pp. Baltimore: William Wood & Company. $16.00.

French's Differential Diagnosis . . .; almost it needs no review! What a name and what a book to ponder on! It is surely a medical classic and if less expensive would rest on every student's and practitioner's bookshelf together with Osler's volume. Since its first printing in 1912, how many generations of medical students have industriously conned its tables of symptoms and differential signs; how many patients have benefited by the knowledge the practitioner has gleaned from its well-written pages.

It is an encyclopedic work, not the least feature of which is the readiness with which any symptom, however obscure, can be referred to in the truly remarkable index of 218 pages. The symptoms are, moreover, alphabetically arranged in the body of the work and well and fully described in systematic form. Discussion of differential diagnosis proceeds logically out of the presenting symptoms as they appear to the examining physician as he tries to solve the riddle of the patient at hand. Despite its profound erudition, the practicality and readability of the work is amazing and in keeping with the best traditions of the British school of writing. Parenthetically, it might be said that we in this country have yet to develop the smooth and lucid style of our English cousins. Are we becoming too scientific for a good literary style?

French's Differential Diagnosis is more than a mere diagnosis or classification of symptoms. In its pages may be found the equivalent of a volume on clinical pathology, another on dermatology, with good measures thrown in of neurology, surgery, gynecology, and ophthalmology. Most of the laboratory tests are fully described and well illustrated. The exception which of course proves the rule is concerned with the blood cells. The sections relating to anemia, leukopenia, and so forth, may well be said to be archaic and might have been written twenty years or so ago. Aplastic anemia, for example, is considered under pernicious anemia. There is still a good deal said of that outmoded disease chlorosis and no mention of chronic hypochromic (iron deficiency) anemia. The term "large hyaline corpuscle" has not yet been superseded by the universally used word "monocyte," nor is there any mention of the hematocrit, mean corpuscular volume, Price-Jones curve, average red cell diameter, Schilling hemogram, the blood platelet count, and so forth, despite the importance of these diagnostic points in the diagnosis of a hematological problem. Nor is there any mention of the sedimentation rate which is now so widely used, both in diagnosis and prognosis. Many methods are described for the minute study of the urine but not a single one is given for the determination of the amount of hemoglobin in the blood. The little section on agranulocytosis might be criticized since one reads that "The outlook is grave and the blood counts not really important . . .; hence the name of this infective and fatal form of sore throat."

The editor states in his preface that "many tests have been omitted purposely, on the ground that, as laboratory methods, their bed-rock reliability has not yet been established . . ." In another place, he says ". . . technique has become almost too perfect; for when clinical methods become too delicate they begin to lose some of their clinical value." This is undoubtedly true, but the editor will agree that in a thorough revision, one expects to find methods now commonly in use in most medical centres. It might have been worth while to place on the editorial staff someone with a good knowledge of things hematological.

The foregoing might conceivably be classed as captious criticism, and should detract in no whit from the great bulk of the work which one supposes is as near perfection as can be obtained in such a wide and difficult field. The illustrations require special mention. They have not been stinted, either in number or in quality. The almost 200 colored lithographs are beautifully done and approach in quality the best of the German or Italian lithographs. The new reproductions of water color paintings by the artist Thornton Shiells have a delicacy of color which makes them exceedingly lifelike. Indeed, it is the quality and number of the illustrations which chiefly distinguish this edition from its predecessor.

The physician who possesses this remarkable work must undoubtedly learn to prize it as his most valuable medical servant. To the reviewer, it has been a real pleasure to scan again its many pages and to imbibe deeply of the wisdom in the many tables and illustrations.

Urethrography. Folke Knutsson. 150 pp. Stockholm: P. A. Norstedt & Söner. Swed. cr. 12:— net.

This short monograph on "Urethrography" is well presented and is based on urethrograms done on 154 patients in Maria Hospital in Stockholm.

This procedure was carried out on thirty-three patients with normal urethras, eighty-five with inflammatory changes in the urethra and prostate (except tuberculosis), nineteen on cases with prostatic hypertrophy, twelve on postprostatectomy patients and

the remainder on patients with traumatic stricture, tuberculosis of urethra, cancer of the prostate and atrophy of the prostate.

The author has a special 20 cc. urethral syringe attached to a penile clamp. Twenty per cent Iodipin (iodine in oil) is used as the opaque fluid. Films are taken in various positions pre- and post-injection; two anterior-posterior views, one before and one after injection, a left and right oblique view, and a lateral view. The author states that in normal cases, there is never any contrast filling of the glands of Littre, the prostatic ducts or the seminal vesicles. In four cases urethrovenous reflux occurred, i.e., the contrast medium passed into the blood vessels of the penis. This, Knutsson states, is the only dangerous complication which may occur in urethrography.

The only question that can be raised about this well-done bit of clinical research is whether the procedure is of great aid in the diagnosis of urethral diseases. There are many urologists in this country who feel that urethrography is very helpful only in an extremely limited number of cases.

Examination of the Patient and Symptomatic Diagnosis. John Watts Murray. Second Edition. 1219 pp. St. Louis: The C. V. Mosby Company. $10.00.

The constant emphasis by teachers of medicine upon the value of a careful history as an approach to diagnosis is presented in this book in a didactic fashion. The bulk of this large volume is devoted to the connotation of symptoms, first as symptoms per se, and later, as they are encountered in specific diseases.

Unfortunately, the book is marred by a number of errors of omission and commission and many dogmatic assertions which are debatable. Space does not permit more than mention of some of these. Among the omissions is the failure to mention leukemia and agranulocytosis as causes of gangrene of the mouth. Under "Nails" no mention is made of changes caused by hypochromic anemia. Hiccup is omitted as a symptom of diaphragmatic pleurisy. There is no reference to or description of monocytes in the cytology of the blood. The same applies to infectious mononucleosis and aleukemic leukemia. The author accepts the American Heart Association classification of heart disease but ignores the important group of hypertensive heart disease.

The following statements seem queer in a modern textbook: "Cardiac arrhythmia may be due to . . . dyspepsia. Permanent bradycardia is usually associated with coronary sclerosis and myocarditis. Irregularities in sexual life may give rise to heart disease. Sometimes occupations which necessitate out-of-door life and exercise may contribute toward the development of pulmonary tuberculosis, but usually people who live out-of-doors are less likely to develop tuberculosis than are those who do not get the proper amount of exercise in the open air and sunshine. Intercostal neuralgia is at times a precursor of pleurisy and pulmonary disease, but the examiner may find that the supposed intercostal neuralgia is really a more serious disease. Purpura hemorrhagica is both hereditary and congenital."

A further drawback is the attempt, in the latter part of the book, to make this a textbook of medicine. The net result is a woefully inadequate discussion of etiological, pathological and prognostic aspects of disease, the total absence of physiological background and an occasional allusion to therapy.

Its chief value appears to be that the student or practitioner reading it cannot escape the powerful argument that meticulous care in eliciting a history is the sine qua non of medical practice. It also presents in concrete form interesting and important facts which should prove of distinct value to anyone desirous of returning to first principles. From this point of view, it may be regarded as dealing with the groundwork of bedside practice. Beyond that, its deficiencies exceed its value.

The Art of Ministering to the Sick. Richard C. Cabot and Russell L. Dicks. 384 pp. New York: The Macmillan Company. $3.00.

Although this book by Cabot and Dicks is addressed primarily to ministers, and deals chiefly with the duties and opportunities of the minister in helping those who are sick, it should be read by every doctor as well. So clearly and so forcefully do the authors present the psychology of the hospital patient that the reader is made cognizant of many aspects of illness of which hitherto he has been unaware.

The book approaches its problem from several points of view. Throughout its pages there is a philosophy based upon a nonsectarian but active religious faith; this constant stream of the consciousness of man's position in the universe plays about and illuminates all the practical suggestions arising from the authors' experiences with sick people.

The technique by which a minister may render help is given in detail; these suggestions are extremely valuable. Constant emphasis is laid upon the cultivation of the habit of listening and of the use of quietness to calm the patient's mind. The value for the minister of keeping records of cases is stressed, it would seem rightly. The reviewer was particularly impressed with the clarity and logic of the chapters which deal with Operations, the Dying and the Bereaved. There is no false sentimentality here; every word rings true.

In their preface, the authors request reviewers to criticize nine ideas which they have woven into their thesis. To one reviewer at least these ideas appear thoroughly sound.

There is so much in this book that no brief review can summarize its contents. It is at one and the same time an exposition of the philosophy of life, a handbook for all who come into contact with sick people, and a guide to help the patient himself to understand the behavior, often apparently inexplicable, of those who are responsible for his welfare. You will be a better physician if you read it.

Physiology of Love. Paolo Mantegazza. 237 pp. New York: Eugenics Publishing Company.

Mantegazza's "Physiology of Love," written immediately after the publication of Darwin's "Descent of Man and Selection in Relation to Sex," was unquestionably inspired by these books. There is plenty of original thought, however, hidden beneath the flowery language in which Mantegazza writes. In his introduction the author says, "My style assumed a warmth and color unnecessary to my purpose: to stimulate people to reflection."

Without doubt this purpose was achieved when the book first appeared in 1872, but it is questionable whether the modern reader will find it particularly stimulating. The love depicted by Mantegazza is of such high emotional content that it appears unfamiliar to people accustomed to the calmer, more philosophical, love of the present day. Possibly this unfamiliarity may be due in part to racial differences.

"Physiology of Love" should by rights be called "Psychology of Love," for it has but little to do with physiology. The author traces the development of love from its manifestations among plants and animals to those in man; he analyzes its satellite emotions—hate, jealousy, modesty; its connection with the senses, with thought, with chastity.

The two great iniquities of love, according to Mantegazza, are first, impotence, and secondly, prostitution. Although the author excoriated both of these, he believed that prostitution was a necessary evil. "So must we do, until progress will have given all men a home and a woman, until the development of education will have taught many the holy joys of chastity."

There is much wisdom in this classic of fifty years ago, if one does not weary of the bombastic but vigorous style in which it is couched. Many of Mantegazza's suggestions for purifying and ennobling the relations of the sexes are equally pertinent today, but most of the book seems to apply to a type of love which is entirely apart from the sober married love that is the only form recognized in this day and country.

Post Mortems and Morbid Anatomy. Theodore Shennan. Third Edition. 716 pp. Baltimore: William Wood & Company. $9.00.

This book presents the technique for performing postmortem examinations and includes with it a description of the various gross lesions which may be encountered in each organ. The manner of arrangement of the material follows the method used in performing autopsies. It begins with a section on the external examination, primary incision, and the examination of the body cavities. Then sections are devoted to the various systems, each beginning with the technique of dissection, followed by a description of the gross lesions which may be encountered. The discussion of the postmortem technique is brief but concise. Its value is somewhat impaired by the separation of the sections devoted to each organ. There are a few diagrams indicating lines of incision but considerably less than might be useful to the beginner in autopsy technique. Discussion of the various disease processes is presented briefly from the standpoint of pure pathological anatomy. There are numerous photographs of gross lesions. Most of these are good and well selected, though a few represent very questionable examples of the lesions. For instance, fig. 32, replacement fibrosis of the myocardium, appears in the picture to be a healed infarction, and fig. 196, intradural round cell sarcoma, is probably a spinal cord covered by metastases from a medulloblastoma. A valuable addition is a chapter devoted to various types of poisoning and the anatomical lesions caused by each. There is a discussion of the medicolegal autopsy and the preparation of material for presentation at court. The book is intended as a guide for work in the autopsy room. References to important and comprehensive articles concerning the conditions dealt with throughout the book would greatly enhance its value. If there were discussions of etiology and pathogenesis included, the value of the book would be greatly enhanced for students in pathology. As it is, the book is worth while recommending for collateral reading in a course in pathology for students who can afford the purchase of an extra book or two. It does not, and is not intended to, replace textbooks with more complete discussions, especially in the relation of structural changes to altered function. For beginners in postmortem work and for physicians who have had a limited experience but who are occasionally called upon to make postmortem examinations, this book is probably the best of any in English. On the whole, considering its size (700 pages) it is a noteworthy achievement.

A. B. C. of the Endocrines. Jennie Gregory. 126 pp. Baltimore: The Williams & Wilkins Company. $3.00.

This very ingenious and quite amusing book consists of an attempt to depict the action and interrelation of the various endocrine glands by means of schematic diagrams. It is in the style, so popular now, of the pamphlets produced by various drug houses to advertise their endocrine products. The book was written to be a useful addition to the library of the medical student and general practitioner, of workers in physiology and biology generally and of the intelligent general reader. In the opinion of your reviewer it is on the shelves of the last group only that the book deserves a place. The individual actually taking care of patients and giving opinions concerning endocrine matters must not depend on kindergarten charts for his knowledge. The author is to be congratulated on her ability in carrying through her project. The feasibility of her project, however, remains a question.

Food, Fitness and Figure. Jacob Buckstein. 252 pp. New York: Emerson Books, Inc. $2.00.

After reflecting on the title, one peruses this book with the expectation of finding it like many others but is agreeably surprised to discover that it is not; and instead is absorbingly interesting. This is because the subject matter is often illustrated by the relation of historical incidents and scientific anecdotes. One of these refers to Eijkmann's discovery of the cause of beriberi. The doctor, stationed in a prison camp in Java, hired a native boy to feed his pigeons, and from time to time gave him money to buy rice for this purpose. The boy, however, got the steward of the camp to give him the rice, and put the money in his pocket. This rice was polished, and the birds, like the inmates of the camp, soon developed beriberi. When the disease among the birds was at its height, the steward went away on leave; and the boy was obliged to buy rice in the market. This happened to be unmilled and when it was fed most of the birds recovered. While such anecdotes make the text entertaining, there is besides real substance in the subject matter; as such chapters as "The Human Machine," "Food and Physical Development," "How the Vitamines Guard Our Health," "The Story of Milk, Cheese, and Butter," "The Normal Diet," "Fad and Fancy about Food," "Vegetarianism," "Fasting," and "The Problem of Weight Control" indicate. In the appendix, the meals to consume to lose, to maintain, or to gain in weight are recorded for a fortnight; as well as the customary charts and tables of food values, and the standard weights of men and women. While the book was written primarily for the laity, nurses, medical students and physicians should find it entertaining and instructive, and it should enhance the library of every dietitian.

Roentgenographic Technique. A Manual for Physicians, Students and Technicians. Darmon Artelle Rhinehart. Second Edition, Thoroughly Revised. 431 pp. Philadelphia: Lea & Febiger. $5.50.

This, the second completely revised edition, represents a modern conception of roentgenographic technique and roentgen ray machines. The author presents experiments and complete explanations of physical factors so that the technician or physician may readily understand why certain procedures for the production of the best roentgenograms are advisable, and be able to carry them out. Since the technical problems are intimately related to disease conditions, some of the more important of these are accurately, but briefly, discussed. The methods of preparing patients for the various examinations and the step-by-step procedures for doing them will be found especially valuable aids to those who are not already thoroughly experienced.

This volume of 431 pages, and 183 illustrations, fills the gap between the textbooks on roentgenography and some of the more readily usable, but inadequate small volumes on roentgenographic technique.

Transactions of the American Association of Genito-Urinary Surgeons. Volume XXVIII. 428 pp. Saint Paul and Minneapolis: The Bruce Publishing Company.

These transactions are composed of thirty-one original papers, and discussions on them, given by the members of this senior society (about sixty active members) of the genito-urinary surgeons of the United States of America and Canada at their annual meeting in 1935.

The papers run the gamut of genito-urinary surgery, from reports of rare or interesting cases, the like of which might never be encountered in a lifetime of practice, to papers which are thoughtful steps in the investigation, analysis and elucidation of general principles of fundamental importance. A good example and the paper which made the greatest appeal to the reviewer was one which showed in a convincing manner the destructive late effects of severe injuries to the kidney, and emphasized the advisability of subsequently studying all cases of suspected kidney injury and, if a persisting abnormality was found, considering operation strongly, in order to avoid the late effects which were shown to be destructive to the kidney.

Taken as a whole these transactions represent the best thoughts of the year of this group of leaders of genito-urinary surgery in America, in which country it is admitted to have attained its highest degree of specialization and development.

The Surgical Clinics of North America. Volume 16, Number I. Chicago Number, February, 1936. 356 pp. Philadelphia and London: W. B. Saunders Company.

The leading feature of this issue is a symposium of seven clinics dealing with the various aspects of cancer of the cervix. Generally approved methods of diagnosis and treatment are presented. A discussion of manipulative surgery with special reference to low back pain and symptomatic sciatica is ably presented by Lewin. He has obtained excellent results in various low back difficulties by manipulation under general anesthesia. The twenty other clinics give concise, practical information on conditions of common occurrence in surgical practice.

The International Medical Annual. A year book of treatment and practitioner's index. Edited by H. Letheby Tidy and A. Rendle Short. 555 pp. Baltimore: William Wood & Company. $6.00.

This volume of 555 pages represents the work of thirty-six leading British physicians who have gleaned the essentials from the medical literature of the year. The material is arranged in encyclopedic form and a general index follows so that it is readily available for quick reference. The generous use of illustrations adds greatly to its value.